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BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

SATURDAY APRIL 9 1955

TABLE OF CONTENTS

The Development of British Endocrinology P. M. F. BISHOP, D.M., M.R.C.P. 865
Pneumococcal Meningitis C. D. R. PENGELLY, M.B., M.R.C.P., M.R.C.P.Ed. 870
Desacetylmethylcolchicine in Treatment of Myeloid Leukaemia B. J. LEONARD, M.D., and JOHN F. WILKINSON, M.D., M.Sc., Ph.D., F.R.C.P., F.R.I.C. 874
Ten-year Recovery from Chronic Lymphocytic Leukaemia MAX SCHOTT, M.D. 877
Uses of Chlorpromazine in Mental Hospital Patients J. LOMAS, M.B., D.P.M. 879
Chlorpromazine in Treatment of Elderly Psychotic Women C. P. SEAGER, M.B., D.P.M. 882
L. Canicola Infection Treated by Penicillin J. CROOKS, M.B., F.R.F.P.S., and W. BLAIR, M.B., D.P.H. 885
Polyagglutinability of Human Red Blood Cells SANTOSH MITRA, M.B., and PROBHAT CHOUDHURI, M.B. 887
Varicoceles of the Round Ligament in Pregnancy, Simulating Inguinal Herniae J. S. TOMKINSON, M.B., F.R.C.S., M.R.C.O.G., and W. R. WINTERTON, M.B., F.R.C.S., F.R.C.O.G. 889
The Symmetrical Form of Status Bonnevie-Ullrich (Turner's Syndrome) J. B. BARLOW, M.B., and S. E. LEVIN, M.B. 890

MEDICAL MEMORANDA
"Primary Myxoedema" in a Man of 30. F. R. M. YOUNG, M.B., B.S. 892
Ventricular Tachycardia following Exercise in a Case of Angina Pectoris. R. BRUCE, M.B., B.S. 892
Grafting of Finger-nails. C. R. MCCASH, Ch.M., F.R.C.S.Ed. 893

BOOK REVIEWS 894

REFRESHER COURSE
Diabetic and Insulin Coma. J. D. N. NABARRO, M.D., M.R.C.P. 902

GENERAL ARTICLES AND NEWS
ADVANCES IN CARDIOVASCULAR SURGERY 904
DOCTORS AND THE PRESS 906
REPORTS OF SOCIETIES 907
MEDICAL NOTES IN PARLIAMENT 917
MEDICO-LEGAL 919
VITAL STATISTICS 920
MEDICAL NEWS 921
QUESTIONS AND COMMENTS 923

OBITUARY
H. M. J. Perry, C.B., O.B.E., F.R.C.P. 915
R. G. Ladkin, M.B.E., B.M., D.P.H. 916
F. H. Scotson, M.B., F.R.C.S. 916
Neil McLean, M.B., D.T.M., D.T.H. 917

LEADING ARTICLES
Noradrenaline 896
Castration of Sex Offenders 897

ANNOTATIONS
Pure Red-cell Anaemia 898
Seasonal Incidence of Peptic Ulcer 899
This Year's Bill 899
Cerebral Basis of Memory 900
Sucrosuria 900
Electrical Activity of the Uterus in Labour 901

CORRESPONDENCE
Heroin. A. H. DOUTHWAITE, M.D. 907
Chicken-pox. J. F. WARIN, M.D.; M. ASTON KEY, M.D. 908
Natural Childbirth CONSTANCE L. BEYNON, F.R.C.S.Ed. 908

SUPPLEMENT
Full Contents on First Page of Supplement
Conference of Honorary Secretaries 157
Consultants and Specialists 159
Correspondence:
Reform of Association's Constitution. V. COTTON-CORNWALL, M.D. 163
Dispensing Doctors. J. A. RICHARDS, M.R.C.S. 163

CORRESPONDENCE—*cont.*
Cervical Cancer. W. I. B. ONUIGBO, B.Sc. 908
Injection Technique. K. D. SALZMANN, M.D. 909
Dermatomyositis. A. BIGHAM, M.D. 909
Grants for New Hospitals. R. S. MURLEY, F.R.C.S. 909
Post-maturity and Asphyxia. H. S. RUSSELL, M.D. 909
Post-puerperal Recurrent Depression. R. GREENE, D.M. 909
Puerperal Depression. K. A. EXLEY, M.D. 910
Low Back Pain. J. H. KELLGREN, F.R.C.P. 910
Pre-employment Examinations. R. WEST, M.R.C.S. 910
Clinical Board Meetings. M. C. LATHAM, M.B. 910
Peptic Ulcer. S. H. F. HOWARD, M.B. 910
Bolus Obstruction. G. E. ALLIN, M.D., and J. G. BRICE, F.R.C.S. 910
Boyle's Machine. J. A. MCNEILLY, M.B. 911
Fluoridation of Water. N. J. AINSWORTH, F.D.S. R.C.S.; E. EYNON VAUGHAN, M.B. 911
Hydrocortisone. S. EDEN, M.R.C.S. 911
Tuberculosis. E. A. CAMERON, M.B. 912
National Formulary. W. N. LEAK, M.D. 912
Epilepsy. D. J. ADDERLEY, M.R.C.S. 912
Vaginal Discharges. ELIZABETH GOURLAY, M.D. 912

Letters on other subjects on pp. 913-915

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY APRIL 9 1955

THE DEVELOPMENT OF BRITISH ENDOCRINOLOGY*

BY

P. M. F. BISHOP, D.M., M.R.C.P.

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Few, I suppose, to-day would deny that endocrinology is a branch of the biological and medical sciences, integrated as a coherent whole to form the subject of textbooks, journals, and societies, and indeed to constitute the professional vocation of a small group of workers who call themselves endocrinologists. Nevertheless it has from the beginning so permeated many other branches of science and medicine as to become an integral part of them. This it will continue to do more and more as the subject unfolds under the warm sunshine of advancing knowledge. Thus it is physicians and physiologists, biologists and biochemists, pathologists and pharmacologists who by their contributions have founded and established endocrinology so that its study and practice have now become essential not only to their own but to other specialties. Should this need, however, be neglected, not only will their own branches of science and medicine suffer, but endocrinology will wither.

British workers have played a distinguished part in the development of endocrinology both in the past and during the present generation, and to-day, with a journal, a society, and a section at the Royal Society of Medicine, endocrinology in this country would seem to flourish and prosper and to be firmly established. Will it continue so in the future? This is the theme I wish to develop.

"Internal Secretions" and "Hormones"

So far as I can discover, the earliest British contributors to endocrinology were Thomas Willis and Richard Lower, both of whom hinted at the possibility of some mechanism of internal secretions. Willis was at school in Oxford and became batteler to a canon of Christ Church and thus matriculated from "the House" in 1636 and took the degree of B.M. ten years later. He was a contemporary of Robert Boyle, John Locke, and other future Fellows of the Royal Society, which received its charter in 1662. When the monarchy was restored Willis was rewarded for his loyalty by being appointed Sedleian Professor of Natural Philosophy at Oxford. During the time he held this chair he wrote much on anatomy, describing of course, among other things, the circle of Willis, and taught a number of students who were subsequently to become famous, such as Christopher Wren. In 1666 he moved to London and built up a lucrative practice. His reputation is difficult to assess. Was he the inventor of the nervous system, the founder of biochemistry (he tasted the urine for diabetes), the peer of Sydenham, Heberden, and Bright, or a parasite living on his pupils' ideas? † It is said that he refused a knighthood because he had been declared by the Merry Monarch to have killed more of his subjects than an invading army. Richard Lower, his pupil, who may well have inspired some of his ideas, including those concerning internal secretions, followed Willis to London in 1666 and eventually became the "most noted physician in Westminster and London" and a confidant of Nell Gwynne. He fell foul of the King, however, and his practice and reputation suffered accordingly. In 1675 he was expelled from the Royal Society, probably for not paying his subscription. Nevertheless he was one of the many physicians who attended the royal deathbed and tortured the wretched Charles, as Macaulay says, "like an Indian at a stake," while he was being "a most unconscionable time a-dying." The first contributors to British endocrinology were therefore colourful, successful, and worldly.

Though endocrinology made few advances during the next 200 years, the conception of internal secretions kept recurring, and George Gulliver, who enjoyed the curious distinction of being surgeon to "the Blues" as well as a Fellow of the Royal Society and a Foundation Fellow of the Royal College of Surgeons, was one of those who played upon this theme by postulating in 1840 that the adrenal glands elaborate a substance which they discharge into the venous blood. The term "internal secretion" was first used by Claude Bernard in a lecture at the Collège de France in 1855, but the word "hormone" was introduced half a century later by Bayliss and Starling. In 1902 they discovered secretin, and felt that its production in one part of the body and its transport to other parts on which it effected changes were not adequately described by calling it an "internal secretion." In their search for a more appropriate term the word "hormone" was suggested, and Starling used it in 1905 in his Croonian Lectures at the Royal College of Physicians. Starling had carved out a distinguished career for himself in the Physiology Department at Guy's, but as the authorities were unwilling to give him full control of the department he left in 1900 to become Jodrell Professor of Physiology at University College. He was succeeded at Guy's by M. S. Pembrey, who from the first took undisputed command of his department. Two years earlier Guy's had lost another distinguished physiologist through inadequately defining his ultimate prospects, for Gowland Hopkins had been enticed

*Based on the Presidential Address to the Section of Endocrinology of the Royal Society of Medicine, delivered on October 27, 1954.

†Sir Charles Symonds, in his recent Harveian Oration (*British Medical Journal*, 1955, **1**, 119), has refuted this suggestion and has borne testimony to Willis's high repute.

to Cambridge by Michael Foster to undertake research in chemical physiology. I mention these facts because they are relevant to my theme.

History of British Endocrinology

The history of endocrinology consists of accounts of the achievements of men who did not call themselves endocrinologists, but were physicians, therapeutists, chemists, pharmacologists, pathologists, and experimental physiologists.

Physicians

From the physicians I choose Addison and Gull, for the circumstances leading up to the descriptions of Addison's disease and myxoedema are characteristic of the atmosphere of the second half of the last century when men had nothing but their eyes, their ears, their finger-tips, and their clinical sense to rely upon. Thomas Addison had spent all his life studying disease at the bedside and in the post-mortem room before he published, at the age of 62, his celebrated monograph in 1855. He was a distinguished dermatologist, and it was under his direction that Joseph Towne modelled in wax the superb collection of specimens of skin disorders which are still to be seen in the Gordon Museum at Guy's Hospital. He had long been intrigued by the morbid state characterized by "anaemia, general languor and debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change of colour in the skin, occurring in connexion with a diseased condition of the suprarenal capsules." Six years previously he had communicated a paper concerning "a remarkable form of anaemia" occurring in patients the whole surface of whose bodies "bears some resemblance to a bad wax figure." Addison wrote sparingly, and it must have taken considerable persuasion on the part of Samuel Wilks, his junior colleague, to get him to produce the finely worded and beautifully illustrated monograph which is to-day such a highly treasured gem among the exhibits of British endocrinology. Unfortunately Addison was to derive little pleasure or satisfaction from it. It is true that Trousseau, during the next year, hailed the monograph and christened the condition Addison's disease. It is also true that, after reading Addison's monograph, Brown-Séquard, later to become physician to the National Hospital for Nervous Diseases, Queen Square, an F.R.C.P. and F.R.S., founded experimental endocrinology by removing the adrenals from a curious assortment of animals and by deducing from the consequently high mortality rate that these glands were essential to life. Nevertheless the medical fraternity at Edinburgh, where Addison had obtained his M.D., would not acknowledge the disease, and two or three papers read before the Medico-Chirurgical Society were not accepted for publication in its *Transactions*. Addison was deeply hurt by this, as he had not long before been president of the society. In 1860 he retired from public life and his beloved Guy's, and shortly afterwards committed suicide.

How different was the background of Gull's disease! In 1850, at a meeting of the Medico-Chirurgical Society, with Addison in the chair, Thomas Curling, a surgeon at the London Hospital, reported two cases of sporadic cretinism with absence of the thyroid gland. No one paid much attention, and it was 21 years before a further five cases of sporadic cretinism were reported to the same society by Hilton Fagge, of Guy's Hospital, ironically with Curling himself in the chair. Fagge recalled Curling's cases and the fact that the thyroid was absent, giving credit to his senior colleague and late teacher, Dr. Gull, for having acquainted him with the principal features of the condition. One of Fagge's patients was obviously suffering from juvenile myxoedema, and this led him "to speculate as to what characters would be present, should the disease (if that be possible) arise still later in the course of adult life." Two years later, in 1873, Sir William Gull read a paper to the same society "On a cretinoid state supervening in adult life in women." In it he described five cases, referred to Fagge's paper, and expressed the belief that these cases were examples of the condition which Fagge had predicted. Gull's paper was brief, and would probably have attracted little attention but for the forcefulness of his character and the fact that he was at this time the most famous physician in the country. Two years previously he had been called in by Sir William Jenner to attend the Prince of Wales, who was suffering from typhoid fever. Seeing that the Queen had lost her beloved husband from the same complaint, it is understandable that when the Prince recovered Gull received not only the heartfelt thanks and gratitude of the nation and the Queen but also a baronetcy. Gull resigned from Guy's at the age of 50 to attend to his busy practice, and died in 1890 following the third of a series of cerebral haemorrhages. On recovering from the first he is said to have remarked, "One arrow has missed its mark, but there are more in the quiver." He left £344,000.

It was, however, William Ord, of St. Thomas's Hospital, who in 1877 gave a full and classic account of the condition and called it "myxoedema." During the next five or six years studies were being made on the Continent of the results of total extirpation of goitrous thyroid glands, and Sir Felix Semon, the laryngologist, on reading Kocher's paper on "cachexia strumipriva," recognized in the description the classic picture of myxoedema, and drew the attention of the Clinical Society of London to the matter. Though Semon's idea that cachexia strumipriva, myxoedema, and cretinism were all due to the same cause was at first ridiculed, eventually the Clinical Society set up the Myxoedema Committee in 1883, with Ord as chairman and Sir Victor Horsley as one of the members. Semon was obviously more familiar with the Continental literature than most of his colleagues, for he was in fact German, and when he came to this country in 1875 he spoke hardly a word of English.

Therapeutists

Treatment, other than empirical quackery, was practically non-existent in those days, and in endocrinology the first to succeed in carrying out a rational form of therapy was George Murray, of Manchester. Here is Sir Walter Langdon-Brown's description of what happened, as recounted to him by Murray himself. At the time of the setting up of the Myxoedema Committee there was a tendency to regard myxoedema as a failure of excretion, hence the patient's bloated appearance. Murray, however, after consulting Horsley, with whom he had worked at University College Hospital, suggested it was due to loss of an active internal secretion; and in 1891 he demonstrated a case of the disease to the Newcastle and Northumberland Medical Society and announced that he proposed to treat it by means of an extract of thyroid gland. A senior member of the society said that it would be just as sensible to treat a case of locomotor ataxy with an emulsion of the spinal cord. Murray arranged with a slaughterhouse to be allowed to dissect out sheeps' thyroid glands, of which he proposed to make an extract. The Newcastle Medical School refused to give him facilities for this, but Armstrong College provided him with a room in which to prepare his extracts. Towards the end of that year he triumphantly demonstrated the same patient, now an active and sprightly woman of 46 as the result of injections of his extracts, to the same society. The patient lived to be 74, by which time she had received the equivalent of 870 sheeps' thyroids.

Murray was, of course, lucky, for a crude extract of sheeps' thyroid glands is as good a therapeutic agent for thyroid deficiency as any other. The therapeutists of the present generation usually have to rely upon the physiologist or the chemist to supply them with their active principle. Thus Lawrence, the pioneer and leading exponent of the treatment of diabetes in this country, had to wait for Banting and Best to introduce insulin before his own life could be saved and he could alleviate the sufferings of so many diabetics during the past 30 years. It was necessary for Reichstein to synthesize deoxycorticosterone acetate before

Leonard Simpson could apply it to the treatment of Addison's disease; and until Dodds had made stilboestrol available oestrogen therapy was virtually ineffective.

Chemists

Chemists, indeed, have played a particularly distinguished part in the history of British endocrinology, as the following examples will show.

On Christmas Day, 1914, a pure, crystalline, and physiologically active protein was isolated from the thyroid gland by the American chemist E. C. Kendall, who, believing that the essential component was oxyindole, christened it "thyroxyindole," which was later shortened to "thyroxin." (The terminal *e* was added to conform to the British system of nomenclature of this class of compound.) In 1926 Harington showed that the active principle was a derivative of tyrosine, indeed a condensation product of 3 : 5-diiodotyrosine, and not of indole, and in 1927 Harington and Barger synthesized thyroxine. It is peculiarly fitting, therefore, that it was in Sir Charles Harington's laboratory that Dr. Rosalind Pitt-Rivers conducted the studies which led to the realization that triiodothyronine is in fact the true hormone of the thyroid gland. By 1929 and 1930 pure crystalline oestrogens were being extracted from the urine of pregnant mares, and G. F. Marrian succeeded in obtaining oestriol from human pregnancy urine. In the same year Marrian isolated pregnanediol, the inert urinary metabolite of progesterone, subsequently to be isolated in pure crystalline form five years later. The elucidation, in 1932 and 1933, of the structure of the *cyclo*pentenophenanthrene ring system cleared the decks for an intensive chemical study of the steroids, including the sex hormones, in which an important part was played by J. W. Cook and his collaborators, who were largely responsible for determining the structure of the natural oestrogens. Struck by the existence of no fewer than five natural oestrogenic substances, Dodds and his colleagues began to wonder how specific was the molecular structure for oestrogenic activity, and they soon found a compound, 1-keto-1:2:3:4-tetrahydrophenanthrene, which did not contain the *cyclo*pentenophenanthrene skeleton but which was weakly oestrogenic. They subsequently established the fact that the phenanthrene structure was not essential for oestrogenic activity, and they eventually tested the potency of the very simple compound anol (*p*-hydroxypropenyl benzene) and found it to be highly active. However, when attempts were made to repeat the work, some batches of anol were found to possess only very slight activity, and it was obvious that the activity in the first batch must have been due to a contaminant. The work was continued in collaboration with Sir Robert Robinson, and it was shown that the active compound was in reality 4 : 4′-dihydroxy-α-β-diethylstilbene. The introduction of this cheap and highly potent oral compound completely revolutionized oestrogen therapy.

In the androgen field Leonard Simpson, Alison Macbeth, and de Fremery had reported abnormal quantities of male hormone in the urine of certain cases of virilism from 1933 onwards, but the chief credit for developing a reliable and accurate method of estimating urinary neutral 17-ketosteroids belongs to Callow. It is of some interest to note how this came about. In 1936 Professor A. W. M. Ellis (now Sir Arthur Ellis), of the London Hospital, appeared before the Hormones Committee of the Medical Research Council and pressed strongly for the establishment, under the Council's auspices, of an endocrine laboratory institute in which hormone assays and estimations could be carried out to assist clinicians in the diagnosis and treatment of endocrine disorders. The Committee considered the proposal and decided that a useful start could be made by trying to find a method of determining the urinary metabolites of the androgens produced by the gonads and adrenal cortex. The task was placed in the capable hands of Dr. R. K. Callow, and his staff was augmented by an additional biochemist, whom he subsequently married. Callow and his colleagues modified the Zimmermann colorimetric method for determination of urinary androgens and put it on a secure basis.

The most recent chemical achievement of which British endocrinologists may be proud is the discovery by S. A. Simpson, J. F. Tait, and H. M. Grundy of the very potent adrenocortical hormone, aldosterone.

Pharmacologists

Pharmacologists have also made valuable contributions to British endocrinology. Dr. George Oliver, a physician who practised in Harrogate during the summer months, had gained the impression that patients suffering from low blood pressure would derive benefit from injections of an extract of the adrenal gland. Trying this out on his son, he thought he detected a contraction of the radial artery. In considerable excitement he rushed up to London to tell his friend Professor Schäfer (Starling's predecessor in the Chair of Physiology at University College) about it. Schäfer was actually conducting an experiment which involved measuring the blood pressure of an anaesthetized dog, and, polite though incredulous, he injected some of the extract into the animal and was astonished to see the mercury almost shoot out of the top of the manometer. The date was 1894, and in the following year Benjamin Moore, working in Schäfer's laboratory, correlated this pressor substance with the adrenomedullary chromagen. Later adrenaline was isolated and its relationship with the sympathetic nervous system remarked upon. A little later still Sir Henry Dale pointed out that noradrenaline reproduced the actions of the sympathetic impulses with even greater fidelity. In 1906 W. E. Dixon obtained from a heart which had been subjected to vagus stimulation an extract which inhibited frog's heart muscle. This substance, subsequently known as acetylcholine, was discovered by accident in ergot of rye by Dale and identified by Dale and Ewins in 1914; it was found to be released at parasympathetic nerve-endings by Dale and Dudley in 1929 when, as Sir Henry has modestly put it, they "were looking for something else."

Pathologists

Pathology, perhaps, has contributed surprisingly little to British endocrinology. Nevertheless there are three exceptions. The first is the detailed description of the histology of the thyroid gland by Wilkinson King in 1836. He described the colloid and showed that it passed into the lymphatics and so into the great veins, adding that "whilst the nourishment of a part is indispensable to its existence, the influence which it exerts upon the circulating fluid may be more or less needful for the healthy subsistence of the entire animal"—a prophetic forecast of the principle of internal secretions. King succeeded Thomas Hodgkin as curator of the museum at Guy's at the age of 28, and his literary output was very considerable; but, as Wilks said, "though young he had an aged worn look and a chronic cough," and he died of pulmonary tuberculosis at the early age of 38. The second exception is the description by A. C. Crooke in 1935 of hyaline changes in the basophil cells of the pituitary in cases of Cushing's syndrome, and the third the observation by H. L. Sheehan that the majority of cases of panhypopituitarism are due to post-partum necrosis of the gland and present clinically as cases of secondary myxoedema and not, as described by Simmonds, as pituitary cachexia.

Experimental Physiologists

Last I come to a group of endocrinologists whom I find difficult to classify, and I think perhaps I can best describe them as experimental physiologists. Actually they may be surgeons, like Astley Cooper and Victor Horsley, performing thyroidectomy on puppies or monkeys; or they may be anatomists, like Zuckerman, whose contributions and those of his school have always been careful, painstaking, and prolific, and yet have ranged over a surprising variety of subjects from the menstrual cycle and the functions of the prostate to the interactions of the hypothalamus and the

pituitary; or neurophysiologists, like G. W. Harris, whose studies of the hypothalamus and the pituitary have been outstanding. They may be engaged on agricultural research, like S. J. Folley, whose studies at Reading have laid the foundations of modern lactational physiology. They may be biochemists, like F. G. Young, whose fascinating studies of the role of the pituitary in carbohydrate metabolism have identified the diabetogenic hormone with the growth hormone. Or they may be truly experimental physiologists, such as the late F. H. A. Marshall and his disciple, A. S. Parkes, whose work on the physiology of reproduction virtually created this branch of endocrinology and has certainly maintained its standard unsurpassed throughout the world.

The object of this historical review has been to point out that the contributions of the British school were noteworthy and important and have gained for British endocrinology a high reputation. The following account suggests that that reputation has been maintained during the last quarter of a century.

The "Journal of Endocrinology"

By the late 1930's it was becoming obvious to a few workers actively engaged in various fields of endocrine research that there was a growing need for a journal in which their results could be published. A small group of ten therefore decided to launch a British journal devoted to the publication of original work in endocrinology. Each of these ten individuals having guaranteed a certain sum of money, the *Journal of Endocrinology* eventually came into being. Sir Henry Dale acted as chairman of the committee which conceived, devised, and launched the project, but, at his own request, he was not appointed chairman of the council of management. Dr. A. S. Parkes was accordingly elected to this post, and Professor F. G. Young became the secretary. With Sir Charles Dodds as editor, the first number of the journal was published in June, 1939. It could hardly have appeared at a less propitious moment. Before the next number was printed the second world war had broken out. Many of the journal's subscriptions came from overseas and therefore promptly ceased at the outbreak of hostilities. Had it not been for the subventions granted from time to time by the Royal Society the journal would assuredly have succumbed. Indeed, at one stage during the war the treasurer was obliged, in order to keep the journal afloat, to call upon the guarantors to pay up half the money they had guaranteed. However, it seems to have been endowed with a miraculous buoyancy, and to-day it is a flourishing concern which publishes four or more numbers a year under the editorship of Professor Zuckerman.

The Society for Endocrinology

Once the war was over, one or two members of the council of management felt the need for periodic symposia on endocrine subjects and suggested that a society should be formed to deal with the organization of such gatherings. The council recognized the rapid expansion that was taking place in endocrinology and the desirability of founding a society membership of which should be open to the many workers now actively engaged in the study of this subject. They felt that this society should take over management of the journal, which should become its official publication. The treasurer, however, insisted that the society should repay the guarantors the money they had individually disbursed to keep the journal alive during the days of its financial difficulties. This money having in due course been repaid, the Society for Endocrinology was founded and held its first meeting at Guy's Hospital in July, 1946, when Sir Charles Harington delivered the inaugural address. Dr. Parkes became chairman of the committee of the society and Dr. S. J. Folley the honorary secretary. The society's first symposium was held in December, 1946. Dr. Folley became chairman of the committee in 1951, and with the two present secretaries, Professor C. H. Gray and Professor N. F. Maclagan, has led the society forward to become the flourishing and respected body that it now is, upholding the highest traditions of academic endocrinology, and enjoying a reputation certainly equal to that of any society of endocrinology throughout the world.

The Section of Endocrinology of the Royal Society of Medicine

In the meantime the clinicians were not inactive. Towards the end of 1944 Dr. Raymond Greene was exploring the possibilities of establishing a Section of Endocrinology of the Royal Society of Medicine and was not finding his task easy. There were some who disapproved of carving another slice off the body medical, and there were others who felt that the creation of a Section of Endocrinology might deprive existing sections of many subjects that they themselves would like to discuss. There were still others who felt that clinical endocrinology was not yet based on a scientific foundation, that most clinical endocrinologists were quacks, and that a Section of Endocrinology would become a sounding-board for their "hot air." On the other hand, Dr. Greene had one or two loyal supporters, particularly Mr. L. R. Broster, who was able to plead the case before the Council of the Royal Society of Medicine. Thus it is almost entirely due to these two enthusiastic pioneers that this section came into existence on January 26, 1946, exactly six months before the Society for Endocrinology held its inaugural meeting. The first president of the section was Sir Walter Langdon-Brown, the two vice-presidents were Mr. Broster and Dr. Gardiner-Hill, and the senior secretary was Dr. Raymond Greene. Indeed, the new section emerged as such a smart equipage that a certain wit christened it "the Section of West-Endocrinology." Sir Walter Langdon-Brown was unfortunately prevented by illness from making a personal appearance before the section, and his presidential address was read for him by Dr. Raymond Greene. On the death of Sir Walter, Mr. Broster became president.

The section flourished from the start, and its meetings were attended by large gatherings which filled the Barnes Hall. Almost immediately all resistance, resentment, and opposition disappeared. The section has always been on the most cordial terms with the Society for Endocrinology, and during the year 1948–9 Dr. Parkes was president of the Section of Endocrinology and chairman of the committee of the Society for Endocrinology. From time to time the section and the society have held combined symposia, and the council of the one and the committee of the other have on occasions met together—for instance, when they asked the Medical Research Council to consider providing facilities for certain laboratory investigations, such as urinary hormone assays, to clinical departments which were unable to have these carried out in their own hospitals. As the result of this approach the Medical Research Council set up a Clinical Endocrinology Committee, which has, among other things, published a standard method of determining urinary 17-ketosteroids. It has also made arrangements to distribute certain steroid reference standards otherwise difficult to obtain. In 1952 the section and the society set up a committee under the chairmanship of Mr. Broster to consider how best to encourage progress in endocrinological research in this country in the future.

The Addison Lecture

As the result of a benefaction to the medical school by one of its old students, Guy's Hospital established an annual lecture to commemorate the part played by Thomas Addison in the foundation of modern endocrinology. The inaugural Addison Lecture was delivered by Sir Charles Dodds in 1946. It has been the custom to select the lecturers alternately from this country and from overseas, and the subsequent lecturers have been Professor E. B. Astwood, of Boston; Sir Henry Dale; Professor G. W. Corner, of Baltimore; Professor F. G. Young, of Cambridge; Professor T. Reichstein, of Basle; Professor S. Zuckerman, of Birmingham; and Professor Lawson Wilkins, of Baltimore. Among

those who have taken the chair at these lectures have been Sir Charles Harington and Dr. E. D. (now Lord) Adrian.

Whither Endocrinology?

At the present time clinical endocrinology has not acquired the status of a specialty to the same extent as has neurology or orthopaedic surgery or psychiatry or paediatrics; the number holding appointments on hospital staffs as endocrinologists can be counted on the fingers of one hand. But, with due respect to the other three, it is fair, I think, to say that this small handful cannot claim the credit for the high record in which British endocrinology is held. As I have already pointed out, there are anatomists, experimental physiologists, biochemists, clinical pathologists, pharmacologists, therapeutists, physicians, surgeons, and even professors of social medicine, who by their research work, their writing, their teaching, their inspiration, and their flair for organizing have raised its standard and made its great reputation.

How can this be maintained? How are future scientists to be trained in, and future doctors to be taught, endocrinology? Above all, what inducements exist at the moment, or are likely to arise in the near future, to attract recruits into endocrinology? Is there to be an Institute of Endocrinology established for postgraduate training? I think not. To be comprehensive, its laboratories, its wards, its clinics, and its specialist departments for the study of diabetes and other metabolic disorders, thyroid disease, paediatrics, neuro-endocrinology, gynaecological and obstetric endocrinology, let alone the more abstruse biological and biochemical research, would spread and sprawl to such an extent that if grafted on to a certain famous postgraduate hospital they would land up in the neighbouring gaol. Furthermore, one could not hope to concentrate the present generation of established endocrinologists in such an institute. Most of them are comfortably ensconced in the departments they have already built up for themselves through their own enterprise and the good will and personal interest of their colleagues. In fact such centralization would be a retrograde step. Regionalization is the modern policy of medical planning.

Is there to be a special course in endocrinology for premedical students, a diploma in endocrinology, a College of Endocrinologists? Again, I think not, for endocrinology is not a pigeonhole specialty, but rather a cross-section of the biological sciences and of medicine, surgery, and gynaecology. We who are specially interested in endocrinology do not want to confine it to ourselves; we want to spread our gospel. We want to collaborate, not to insulate; to co-operate, not to isolate.

Nevertheless we are firmly convinced that endocrinology is an established, respectable, orthodox, and rapidly expanding biological and clinical science. We would do much to prevent it from being stifled, swallowed up, derided, or ignored. So what must we do? Those of us who hold appointments in undergraduate teaching hospitals must select from our collection a few only of our most classic cases of common endocrine disorders and demonstrate them to the students simply and attractively. These demonstrations should be memorable but infrequent, for the medical student has more than enough to learn already, and endocrinology is only a very limited part of that amount. In postgraduate teaching it might be an advantage to arrange a systematic course of lecture-demonstrations given by those who have made a special study of this specialty.

Recruitment

There are physicians and others who are members of the Section of Endocrinology who have established themselves and made their names famous as endocrinologists, whatever they may officially call themselves. There are younger and more junior Fellows of the Royal Society of Medicine who attend the meetings of the section simply because they wish, quite rightly, to broaden their medical education. A few, however, may be genuinely interested in endocrinology and would like to specialize in it, if only they dare take the risk. And the question is, dare they take the risk? Of course, if you want to be successful in life you must always take a risk. You must take a risk if you aspire one day to become a consultant physician, for there are not nearly enough consultant posts in internal medicine to accommodate the many hundreds of hard-worked, underpaid, and well-qualified medical registrars. And you of the present generation live in a competitive age in which only a few can reach the top in whatever walk of life you choose. Nevertheless there *are* sufficient consultant posts in medicine, surgery, obstetrics and gynaecology, neurology, dermatology, ophthalmology, oto-rhino-laryngology, orthopaedics, genito-urinary surgery, paediatrics, anaesthetics, radiology, radiotherapy, and psychiatry to attract recruits who are prepared to spend more years in training for them than they took to become qualified doctors.

But what of endocrinology? There are, I think, opportunities for training. In most schools of medicine there are posts to be held in the departments of clinical chemistry or clinical pathology where the basic technique may be learnt, and there should be vacancies for men so trained to work at registrar level in the departments of those who have established themselves as experts in some branch of clinical endocrinology. Another method—though I am not suggesting that it is necessarily the only method—of obtaining such training has been provided by the Medical Research Council. In 1951 this body launched a scheme of Clinical Research Fellowships. The holder of one of these Fellowships is paid at registrar level and is given the opportunity of acquiring the techniques and disciplines of those basic sciences relevant to his clinical interests, or of working in a department of recognized standing already engaged in clinical research, such as the clinical units of the Universities or the Medical Research Council. If he makes a success of his Fellowship, there is the possibility that he might obtain one of the Council's Rockefeller or other Travelling Fellowships and thus have the opportunity of broadening his outlook by working in the department of some distinguished foreign expert in the particular specialty he has chosen. Furthermore, he may do this without losing his place in the queue, for the Council has insisted on a promise from the applicant's sponsor of an appointment at the end of the training period. But what appointments are, in fact, available at the present moment, either in general clinical endocrinology or in some branch of endocrinology? The answer is, I am afraid, "None." Now this is disastrous, for unless you can offer the trainee some prospects, some goal to aim at after you have so carefully, arduously, and expensively trained him, you will find no recruits, and clinical endocrinology in this country will wither and die.

How is this very serious and urgent situation to be remedied? Not, I think, by setting up a whole crop of new departments of clinical endocrinology, for this would take more time than, in our urgent predicament, we can afford. It would require a large capital grant and a substantial endowment, which are most unlikely to be provided either by the National Health Service or by the University Grants Committee in these stringent times. It would need the greatest good will and active co-operation of the clinical staff of the hospitals in which the new departments are to be set up, and indeed it is very doubtful whether one could "sell" the scheme to medical committees and boards of governors of hospitals, already short of beds and with the present drastic cuts in their maintenance costs, even supposing they were sympathetically attuned to the idea of creating and expanding a new specialty. This does not mean that I do not hope that existing departments of endocrinology will flourish to the mutual benefit of themselves and the hospitals in which they are established, and by their example prepare the way for the foundation of other such departments at the earliest expedient moment. I hope also that existing departments of endocrinology may be given the opportunity of playing their part in training future endocrinologists.

But at the moment, I think, our best chance of overcoming the serious predicament of lack of recruits in endocrinology is to encourage the establishment and expansion of the endocrine aspects of certain branches of the medical sciences which cannot afford to ignore endocrinology if they are to make their proper contributions and retain their high reputation in this age of rapid scientific advances. I will take two examples to illustrate what I mean. The first is paediatrics. Lawson Wilkins has shown the close relationship between paediatrics and endocrinology, and through his inspiration, enthusiasm, and hard work he has made far-reaching contributions, not only to paediatrics, but to endocrinology. He has broadened the scope of paediatrics and, far from snatching the livelihood from the mouths of the paediatricians, he has presented them with a new stock-in-trade, and on account of his work and that of others like him paediatricians throughout the world are being consulted more and more about endocrine problems. If the paediatricians of this country would select and encourage one or two of their promising young registrars and have them fully and carefully trained as endocrinologists, and then be prepared to give them consultant status with charge of beds and full responsibility for the care of patients, I feel sure that this step would redound to the credit of British paediatrics. My other example is gynaecology. In my view there is need for more gynaecological endocrinologists. In the first place, disorders of menstruation constitute a rather complex aspect of applied physiology which can be thoroughly comprehended only by someone with a fair knowledge of general endocrinology and biochemistry, and it is seldom that the gynaecologist has this knowledge. His training and outlook are totally different. The surgical skill and technique of the gynaecologist, the mechanical manipulations of the obstetrician, and the necessarily rapid repetition of pelvic examinations in the out-patient clinic are unlike the careful recording of menstrual cycles and the precise timing in relation to the menstrual cycle of endocrine therapy, familiarity with the dosage, potency, toxicity and efficacy of different preparations, and the complementary activities of the adjoining endocrine laboratory unit. Nevertheless endocrinology is playing an increasing part in gynaecology. Let the gynaecologists single out and encourage a few of their promising young registrars and have them fully trained as endocrinologists, and then appoint them with consultant rank to gynaecological professorial units or special gynaecological hospitals. Then give them an endocrine laboratory, and they will provide an added stimulus to the work and enhance the reputation of the department or hospital concerned.

I have chosen only two examples: I could develop my theme further. Clinical endocrinologists are needed in thyroid clinics, fertility clinics, and departments of internal medicine, rheumatology, urology, dermatology, allergy, and even surgery. They may be purely clinical endocrinologists with a background training in either physiology or internal medicine, or they may be recruited from the ranks of the specialty on to which it is intended to graft endocrinology. In either case they should have full consultant status. This is not, in my view, an unrealistic dream. It needs enlightened boards of governors and tolerant and sympathetic medical committees, and heads of departments with a determination to carry out their plan. Unless in some such way consultant posts are created soon, endocrinology in this country will surely wither.

The *British Journal Photographic Almanac* for 1955 (Henry Greenwood and Co., 5s., or cloth-bound 7s. 6d.) has several articles on recent progress, both in techniques and apparatus, which will be of interest in hospital radiography departments. It is pointed out how much radiography has benefited from new advances in isotope production, and how photochemistry is helping to unravel complex chemical problems. A six-page table gives summary information about materials for medical photography. The photogravure reproductions are excellent.

PNEUMOCOCCAL MENINGITIS

A SHORT SURVEY OF 78 PATIENTS IN THE BRISTOL CLINICAL AREA

BY

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In general the prognosis in pneumococcal meningitis has been poor; indeed, before the availability of the sulphonamides it was almost hopeless, 100% mortality having been recorded by Toomey and Roach (1939) and Silverthorne (1948), and a review of 631 cases from the literature revealed but one survival (Waring and Weinstein, 1948). After the introduction of the sulphonamides the mortality remained at about 60 to 80% (Table I), but marked improvement followed the introduction of penicillin, although very varied results have been reported (Table II). In some the mortality is 20% or less, but the average for the results quoted is 40% (Table II).

TABLE I.—*Mortality of Pneumococcal Meningitis Treated with Sulphonamides Alone (Various Authors)*

Authors	No. of Cases Treated	Mortality
Appelbaum (1945)	139	65%
Dowling *et al.* (1942) ..	72	94%
Hartmann *et al.* (1945) ..	34	63%
Hodes *et al.* (1943)	60	58%
Jackson (1950)	82 (excluding those treated with sulphanilamide only)	79%
Neal *et al.* (1940)	30	67%
Rhoads *et al.* (1940) ..	22	68%
Sweet *et al.* (1945)	40	92%
Walker and James (1945) ..	28 (one patient treated with penicillin)	64%

TABLE II.—*Mortality of Published Series of Cases of Pneumococcal Meningitis Treated with Penicillin*

Authors	No. of Cases	Mortality
Appelbaum and Nelson (1945)	67	61%
Appelbaum *et al.* (1949) ..	125	26%
Bunn and Peabody (1952) ..	20	35% (25% if 2 patients who died during treatment from other causes are excluded)
Dowling *et al.* (1949) ..	87	56%
Feibush *et al.* (1952) ..	22	68%
Galloway and Chambers (1953)	27	33%
Gibson and James (1952) ..	31	10%
Hall *et al.* (1946)	17	24%
Jackson (1950)	51	43%
Lowrey and Quilligan (1948)	17	18%
Nemir and Israel (1951) ..	15 (all infants and children)	7%
Ross and Burke (1946) ..	19	16%
Smith *et al.* (1946)	38	24%
Sweet *et al.* (1945)	16	56%
White *et al.* (1945)	50	64%
Total	602	40%

Present Series

During the period January 1, 1946, to May 31, 1953, pneumococcal meningitis was diagnosed in 78 patients in hospitals for acute cases in Bristol. Hospitals for chronic cases were not included in the survey. A number of recurrences brought the total number of attacks of meningitis to 84, in 82% of which the pneumococcus was cultured from the C.S.F. either in life or at necropsy, and in the remainder it was seen in a stained smear.

Mortality.—Of the 78 patients 38 died, a mortality of 49%. A necropsy was performed on 28 (74%). The mortality calculated according to the number of attacks of meningitis was 45%.

Age Distribution.—The age distribution of the patients in 10-year periods is shown in Table III. In addition the period from birth to 1 year of age is included. The

TABLE III.—*Age Distribution of 78 Cases of Pneumococcal Meningitis in Bristol*

Age	No. of Patients	No. Dying	No. Recovering	Mortality
0–1 *year*	*20*	*7*	*13*	*35%*
0–9 years ..	42	15	27	36%
10–19 ,, ...	6	3	3	50%
20–29 ,, ...	2	1	1	50%
30–39 ,, ...	9	5	4	55%
40–49 ,, ...	3	1	2	33%
50–59 ,, ...	7	7	0	100%
60–69 ,, ...	8	5	3	62%
70+ ,, ...	1	1	0	100%
Total ..	78	38	40	49%

mortality for each age group is shown. Notable features are the relatively large number of infants and children under 10 years old and the steep rise in mortality for those patients aged 50 and over. Only 3 recoveries occurred in 15 patients in the latter group (82% mortality). For infants the mortality was 35%, or rather below the average (49%).

Cause of Meningitis.—In many of the patients there was a demonstrable primary focus of infection, in some it was apparent during life and in others only at necropsy. In a few trauma was the immediate cause and in a large group no cause was found (Table IV). Cases with a clear terminal

TABLE IV.—*Apparent Primary Cause of Meningitis in 78 Patients*

Apparent Primary Cause	No. of Patients	No. Dying	No. Recovering	Mortality
Middle ear or mastoid infection ..	30	12	18	40%
Pneumonia ..	8	4	4	50%
Nasal sinus infection	3	3	0	100%
Panophthalmitis ..	1	0	1	0%
? Bacterial endocarditis ..	1	0	1	0%
Trauma	9	4	5	44%
No cause found ..	26	15	11	58%
Total ..	78	38	40	49%

bronchopneumonia only have been excluded from the "pneumonia" group. In the "trauma" group six had head injuries, in two the meningitis followed nasal operations, and in one it followed a perforating injury of one internal ear.

Level of Consciousness on Admission to Hospital.—In 37 of the attacks the patient was either fully conscious or at worst stuporous on admission to hospital, and death followed in 9 (24% mortality). In 31 attacks the patient was delirious or comatose when admitted and death followed in 19 (61% mortality). In 12 attacks continuous convulsions were occurring at the time of admission and death followed in 8 (66% mortality). (Two attacks occurring in patients transferred to the area for operation and two in patients admitted to hospital for a condition other than meningitis have not been included.)

TABLE V.—*Distribution of Attacks of Pneumococcal Meningitis According to the Length of Illness Before Admission to Hospital**

No. of Days' Illness before Admission to Hospital	No. of Attacks of Meningitis	No. of Attacks with Fatal Outcome	No. of Attacks with Recovery	Mortality
Less than 1 ..	10	7	3	70%
1	18	10	8	56%
2	9	6	3	67%
3	15	1	14	7%
4	5	2	3	40%
5	4	2	2	50%
6	1	0	1	0%
7	7	2	5	29%
More than 7 ..	8	3	5	37%
Unknown ..	3	3	0	100%
Total ..	80	36	44	45%

* Excluding four attacks, two of which developed in patients who were being treated in hospital for another condition and two in patients transferred from outside the area for operation.

Duration of Illness Before Admission to Hospital.—An analysis of attacks according to the number of days of illness before the patient's admission to hospital is shown in Table V.

Treatment

Chemotherapy and Antibiotics

Table VI shows the sulphonamide and antibiotic treatment given. There are four groups: the first, designated "standard therapy," consists of attacks treated with a sulphonamide together with penicillin by both the intramuscular and the intrathecal routes. Group 2, designated

TABLE VI.—*Sulphonamide and Antibiotic Treatment of 84 Attacks of Pneumococcal Meningitis*

Treatment	No. of Attacks of Meningitis	No. of Attacks with Fatal Outcome	No. of Attacks with Recovery	Mortality
1. Standard treatment ..	54	20	34	37%
2. Incomplete treatment ..	14	11	3	79%
3. Additional treatment ..	13	4	9	31%
4. No specific treatment ..	3	3	0	100%
Total ..	84	38	46	45%

Occasionally one of the items of the "standard" treatment was omitted in patients in group 3.

"incomplete therapy," contains those attacks treated as in group 1 but incomplete in some respect—for example, no sulphonamide, no intrathecal penicillin, etc. Group 3 shows those attacks treated as in the preceding groups, but with one or more additional antibiotic. Group 4 shows those attacks not specifically treated.

The additional therapy in Group 3 consisted of intramuscular streptomycin in two attacks, intrathecal streptomycin in two, chlortetracycline (orally) in four, chloramphenicol (orally) in two, and chlortetracycline (orally) with intrathecal streptomycin in one.

The majority of patients receiving penicillin were given an intrathecal dosage of 5,000 to 30,000 units, once or at most twice daily. In two cases 500,000 units was given in error at a single injection and in both death followed within 24 hours preceded by generalized convulsions. Sulphonamides were used as for any acute infection, and intramuscular penicillin was given in a dosage which varied from about 100,000 to 1,000,000 units in 24 hours divided usually into three- or four-hourly doses. In 45 attacks under 250,000 units in 24 hours was given, and in the remaining 39 more than this amount was used. The mortality was 45% in the group receiving the smaller amount and 46% in that receiving the bigger dose. If the 10 attacks in which no penicillin was given intrathecally are excluded from the lower-dosage group the mortality in the remaining 35 attacks was 34%. Two of the patients receiving no intrathecal penicillin recovered.

Surgical Measures

The operation of mastoidectomy was performed five times in the series, being done 38, 8, 7, and 2 days after the patient's admission to hospital in the four cases which recovered. In the one fatal case, that of a baby aged 4 months, it was done on the day of admission. Burrholes were made in the skull for penicillin administration after the development of a block in the spinal theca on three occasions; one patient recovered. In one of the others the meningitis was apparently controlled after this treatment, but the patient remained comatose and died possibly with a cerebral abscess; there was no necropsy. Three further patients were investigated by ventriculography to exclude an intracranial abscess, but none was found. One had developed a right arm paresis which slowly recovered, and the other two were recurrent cases and are mentioned below.

Recurrent Cases

In five patients in the series recurrences occurred. In one, that of a boy aged 8 years when he had his first attack in 1947, recurrences occurred five times, with long intervals between attacks. Only in the first was an infective focus discovered and this eliminated by mastoidectomy. The second patient, a man aged 30, was reinfected through defects in the floor of the anterior cranial fossa. Removal of nasal polypi and a bilateral Horgan's operation were carried out in 1949, following which he had C.S.F. rhinorrhoea. Three weeks after the operation he developed a purulent meningitis from which no organisms were isolated. Two months later a proved attack of pneumococcal meningitis occurred, and after preliminary medical treatment an exploration revealed a hole in the right side of the floor of the anterior cranial fossa which was covered by a graft. After 18 months of good health another attack of pneumococcal meningitis occurred and yet another six months later. In March, 1951, further exploration revealed another hole in the floor of the anterior cranial fossa, this time on the left side, which was also covered by a graft. He remained free from further attacks of meningitis following this, only to die in May, 1953, from a spindle-cell sarcoma arising in his abdominal wall.

The third patient, a lad aged 16, was admitted to hospital with a purulent meningitis the day following a minor head injury in January, 1949; there was no radiological evidence of fracture. No organism was isolated. After a rapid recovery he remained well until 18 months later, when he had a proved attack of pneumococcal meningitis. A good response to medical treatment occurred and he has remained well since.

The fourth patient, a man aged 30, was admitted to hospital with pneumococcal meningitis after a history of 24 hours' headache and vomiting. He was in coma. He responded to treatment and no focus of infection was discovered. He remained well until four years later, when he had another attack, coma occurring only a few hours after the onset of headache. In spite of early treatment he died within 24 hours of admission. Necropsy revealed a purulent meningitis and an astrocytoma of the mid-brain causing obstruction of the aqueduct and internal hydrocephalus. There was no infective focus.

The last patient, a girl aged 16, had a splenectomy for Banti's disease at the age of 12 years and developed a meningitis one year later. No organisms were isolated. An attack of pneumococcal meningitis occurred after another two years (1950) and failed to respond well to medical treatment. She was therefore transferred to the Bristol Neurosurgical Unit for investigation, where ventriculograms were negative and the meningitis slowly responded to continued sulphonamide and penicillin therapy. A relapse occurred as soon as treatment was stopped, but she responded well to chloramphenicol. The presence of an apical systolic murmur in her heart suggested the presence of bacterial endocarditis and she was accordingly given a six-weeks course of penicillin, 2,000,000 units a day. She remained well until 1952, when she died at home after a short illness, possibly another attack of meningitis.

Associated Diseases and Conditions

The meningitis was found in association with other conditions in 10 cases: diabetes mellitus twice, Parkinsonism, cirrhosis of the liver, astrocytoma of the mid-brain, hydronephrosis and chronic pyelonephritis, right upper lobe bronchiectasis, Banti's disease, situs inversus totalis, and familial acholuric jaundice. All except the last two of these patients died.

Discussion

The present series of cases of pneumococcal meningitis is entirely unselected and includes patients already suffering from a serious disease, which accounts for the high mortality. If only those attacks in which full sulphonamide and penicillin therapy was given are considered the mortality is 37% of 54 attacks (Table VI), and, furthermore, excluding those cases in which death occurred within 24 hours of admission to hospital, the mortality becomes 28% of 43 attacks, a figure comparable with all but the very best results (Table II).

Age is a very important factor in relation to prognosis in the disease, particularly poor results occurring in patients aged 50 or more. This is not only the impression from the present series (Table III) but has also been the experience of others (Table VII), although it was not a notable feature of the series of Smith *et al.* (1946). Very young patients had a poor prognosis before penicillin became available (Cooke, 1941; Waring and Weinstein, 1948; Jackson, 1950), but the prognosis for infants when penicillin is used appears fairly good. With penicillin treatment, Waring and Weinstein (1948) noted a 69% recovery for patients under 2 years old (58 cases), while Nemir and Israel (1951) lost only one of nine infants, and Ross and Burke (1946) achieved a recovery of all nine infants. In the present series also the prognosis for infants with penicillin therapy was better than average (Table III).

TABLE VII.—*Relationship Between Age and Mortality Rate in Pneumococcal Meningitis. Percentages Calculated from Figures Given by Various Authors*

Authors	Mortality in Ages (Years)				
	No. of Cases	Under 40	Over 40	Under 50	Over 50
Appelbaum (1945) ..	67	44%	73%	54%	72%
Feibush *et al.* (1952) ..	22	43%	80%	44%	85%
Jackson (1950) ..	125	67%	76%	—	—
Lepper and Dowling* (1951)	43	—	—	23%	41%
Sweet *et al.* (1945) ..	56	68%	89%	—	—
White *et al.* (1945) ..	50	—	—	52%	88%
Present series	78	41%	74%	40%	81%

* Not including chlortetracycline-treated cases.

The commonest predisposing cause of the meningitis in the present series was middle ear and mastoid infection (38%) (Table IV), but in 33% no cause could be found. Pneumonia has often been noted as a common if not the commonest cause of pneumococcal meningitis (Table VIII) but accounted for only 10% of the cases in this series.

Trauma is evidently a rare cause (Tables IV and VIII) but is, however, a very important one, as recurrences are

TABLE VIII.—*Predisposing Cause of Pneumococcal Meningitis Expressed as Frequency Distribution in Percentages to Nearest Whole Number. Collected Figures of Various Authors*

Predisposing Cause	Appelbaum *et al.* (1949)	Dowling *et al.* (1942)	Dowling *et al.* (1949)	Appelbaum and Nelson (1945)	Gibson and James (1952)	Jackson (1950)	Sweet *et al.* (1945)	White *et al.* (1945)	Total, Excluding Present Series	Present Series
No. of cases ..	125	72	87	67	31	125	56	50	613	78
Middle ear or mastoid infection ..	29%	29%	18%	45%	26%	29%	11%	46%	29%	39%
Pneumonia ..	22%	28%*	32%	25%	23%	26%	34%	18%	26%	10%
Fractured skull or other trauma ..	6%	4%	2%	3%	13%		5%		3%	12%
Others	6%	25%	5%	3%	23%	7%	30%	12%	12%	6%
No cause found ..	38%	14%	43%	24%	16%	38%	20%	24%	30%	33%

* 3% had middle ear or mastoid infection also.

apt to occur, especially if the thin floor of the anterior cranial fossa has been fractured. The covering of the damaged bone with a graft of fascia lata proves an effective means of preventing further attacks. Defects in the floor of the anterior cranial fossa causing meningitis may be congenital in origin (Galloway and Chambers, 1953).

Coma and convulsions at the time of admission to hospital indicated a poor prognosis in this series, the difference in mortality between those fully conscious or only stuporous on admission and those having convulsions or comatose being statistically significant. This result might be reasonably anticipated; it was also found by Lepper and Dowling (1951), but was not confirmed by Feibush *et al.* (1952) in a small series of cases.

It is apparent from Table V that those patients who were ill for three days before admission to hospital had the best prognosis. There was only one patient older than 50 years in that group, but even after removing all patients aged 50 or more the mortality for those ill less than three days before admission was 61% (31 cases), for those ill more than three days 24% (21 cases), and for those ill just three days 7% (14 cases). All the fulminating cases are obviously included in the first group, in which 62% were in coma or having convulsions when admitted. Twenty-seven per cent. of the 14 cases ill for three days and 52% of those ill for more than three days before admission to hospital were in coma or having convulsions when admitted. It is probable that more of the last group would have recovered had full medical treatment been started earlier.

Combined sulphonamide and penicillin therapy still remains the treatment of choice in pneumococcal meningitis, and the penicillin should be given by both the intramuscular and the intrathecal routes. Excellent results have been obtained by this method (Ross and Burke, 1946; Smith *et al.*, 1946; Gibson and James, 1952) (Table II). Sulphonamides should be given as for any acute infection, but the daily intramuscular requirement of penicillin is not clear. Smith *et al.* (1946) were using at first about 120,000 units daily in three- or four-hourly doses or by continuous intramuscular infusion, while Gibson and James (1952) were using latterly 1,600,000 units daily. As already shown, in the present series those cases receiving more than 250,000 units daily fared no better than those receiving less, and the two groups appear comparable so far as age distribution and level of consciousness on admission to hospital are concerned. Dowling *et al.* (1949) have said that intrathecal penicillin administration is unnecessary provided that large enough doses are given intramuscularly. They treated 66 cases by the ordinary method and 21 cases without intrathecal therapy and 2,000,000 units of penicillin every two hours intramuscularly: the mortality of the first group was 66% and of the second 38%, results which are not good and can hardly be used as an argument for rejecting intrathecal therapy. Smith (1951) found a clinical and bacteriological relapse in a baby with pneumococcal meningitis when given a non-potent dose of intrathecal penicillin in spite of massive intramuscular penicillin dosage every two hours.

In spite of the 75% cure of 20 cases without intrathecal penicillin by Bunn and Peabody (1952), there is no convincing evidence that intrathecal therapy with penicillin should be abandoned. It should remain part of the routine management in pneumococcal meningitis, and should be given in daily doses of about 20,000 units for about 7 to 10 days or until the meningitis is obviously under control. Much larger doses should not be used, as they are known to produce damage to the spinal cord and cauda equina or even convulsions and death. As little as 50,000 units intraventricularly has produced convulsions (Johnson and Walker, 1945). Gibson and James (1952) thought the dangers were exaggerated and gave even their infants 50,000 units at a single dose.

Although there is no clear-cut evidence in favour of giving very large intramuscular penicillin doses when intrathecal treatment is being given, it is probably wise to give at least 2,000,000 units daily in divided doses with intervals of not more than four hours between injections. Fortunately the pneumococcus is usually highly sensitive to penicillin and does not develop resistance during treatment.

There is no evidence in the literature that treatment with antibiotics in addition to penicillin will improve the prognosis. On the contrary, there is evidence that the addition of chlortetracycline therapy leads to a worsening of the prognosis. Lepper and Dowling (1951) treated 43 cases with the usual intramuscular and intrathecal penicillin and 14 with the addition of chlortetracycline. In the first group 30% of the patients died, and in the second 79%, a statistically significant difference.

Surgical treatment for the elimination of foci of infection in the ears, mastoids, or sinuses was regarded as a mainstay of treatment in pneumococcal meningitis before penicillin was available (Neal *et al.*, 1940; Walker and James, 1945), but with the use of penicillin Smith *et al.* (1946) never found such operations necessary in the acute phase and often not at all. Ross and Burke (1946) found no surgery necessary in their 19 cases. Mastoidectomy was required five times in the present series in spite of penicillin therapy. A certain number of recurrences can probably be prevented by the removal of chronic sepsis in ears, mastoids, and sinuses after treatment of the meningitis.

Burr-holes are made in the skull for the intraventricular administration of penicillin or for the diagnosis of an intracranial abscess. Penicillin may be given intraventricularly if a block with exudate prevents its free access to the brain when administered by the lumbar route. Cisternal administration of penicillin may suffice but does not guarantee that it will reach the ventricles. Spinal block is not common in pneumococcal meningitis. Intraventricular penicillin administration was needed in only two of the last 19 cases of Smith *et al.* (1946) and was required only three times in the present series. Intracranial abscess is also a rare complication. Smith *et al.* (1946) found this only twice in their 38 cases, and in reviewing the literature Waring and Weinstein (1948) found only 3.6% of 386 cases and none in 86 treated with both penicillin and sulphonamides.

Pneumococcal meningitis may complicate other and serious diseases as previously shown, when the prognosis is correspondingly poor. The association with diabetes mellitus and hepatic cirrhosis in this series led to diagnostic difficulties and delay in treatment.

Summary

A short survey of 78 cases of pneumococcal meningitis in the Bristol Clinical Area is presented with a discussion of certain aspects of aetiology, prognosis, and treatment.

The mortality was 49%, or 45% in 84 attacks of meningitis, as there were some recurrences. The cases were unselected, and included those already with chronic and wasting diseases.

It has been shown that the prognosis was much worse in patients over 50 years of age, but that the results in infants and young children were better than the average; also that coma or convulsions occurring at the time of admission to hospital influenced the prognosis very unfavourably.

Middle ear or mastoid disease was the commonest primary source of infection, but almost as frequently no source of infection or other predisposing cause could be demonstrated. Pneumonia was an uncommon source of the infection.

Prognosis was worse in those cases with a period of illness greater or less than three days before hospital admission, presumably because the fulminating cases

were admitted quickly while some of the others were left too late before in-patient treatment was started.

My thanks are due to the consultant medical staff of the Bristol Hospitals for permission to use their records, and especially to Dr. J. Macrae, of the Ham Green Fever Hospital, for his help; to Drs. A. M. G. Campbell and J. K. Lloyd for valuable criticism; and to Dr. G. Herdan for statistical advice.

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DESACETYLMETHYLCOLCHICINE IN TREATMENT OF MYELOID LEUKAEMIA

BY

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AND

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In 1953 Moeschlin and colleagues reported that desacetylmethylcolchicine ("colcemid") had beneficial effects on a group of patients with chronic myeloid leukaemia, while some encouraging results were also noted in a few cases of acute myeloid leukaemia and in two patients in the acute myeloblastic phase of chronic myeloid leukaemia. On the other hand, chronic lymphatic leukaemia failed to respond and might even have been made worse. The profound depressive effects on the granulocytopoiesis were accompanied simultaneously by a reduction in the size of the spleen and an increase in the red blood cell count and haemoglobin values.

Desacetylmethylcolchicine was isolated in a pure form by Santavy and Reichstein (1950) from the mixed alkaloid extract of *Colchicum autumnale* and was found to have a relatively low general toxicity, some 30–40 times less than colchicine (Schär *et al.*, 1954), which, although having a very marked inhibitory effect on cell mitosis, is too toxic for safe clinical use (Jacobj, 1890; Dustin, 1938; Bucher, 1939).

Lichtman (1954) has described in detail the effects of desacetylmethylcolchicine on the blood cellular elements in rabbits and cats, producing a diminution of total leucocyte count in two days after intravenous administration and in 12–14 days after oral treatment. With cessation of treatment the leucocytes rapidly returned to normal levels.

We have been able to repeat the observations of Moeschlin and his colleagues in a series of leukaemias and leukaemoid conditions, and are reporting here some of our results with chronic and acute myeloid leukaemias.

Dosage and Control

The initial oral dose of 3 mg. of colcemid daily was increased after three to four days to a total of 7–10 mg. daily according to the white-cell count. This dosage was continued until the leucocytes dropped to approximately 25,000 per c.mm., and was then stopped for three to four days. A daily maintenance dose of 3–5 mg. was then instituted. Daily white-cell counts, platelet counts, and haemoglobin estimations were performed until the maximal effect on the white cells had been attained; thereafter counts were done twice weekly and finally every one to two weeks.

Chronic Myeloid Leukaemia (8 cases)

Of eight patients with chronic myeloid leukaemia there was a distinct clinical improvement in six (Cases 1–6); their appetites improved, they gained weight and experienced far more energy; their spleens rapidly decreased in size and became barely palpable. In the remaining two (Cases 7

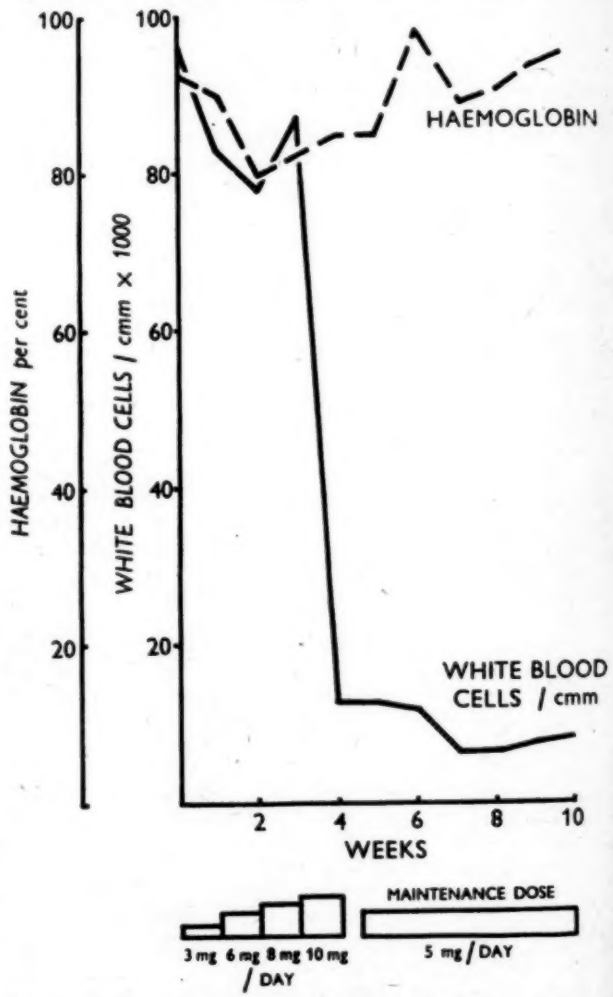

FIG. 1.—Case 6. Effects of colcemid on the total white cells and haemoglobin levels.

TABLE I.—*Chronic Myeloid Leukaemia Treated with Colcemid*

Case	Age and Sex	Before Treatment W.B.C.	Before Treatment Hb	After Treatment W.B.C.	After Treatment Hb	No. of Days of Initial Treatment	Total Initial Course mg.	Max. Daily Dosage mg.	Maintenance Dosage mg.	Effects on Splenomegaly (cm. Below Costal Margin)
1	60 F	136,000	58%	4,100	71%	21	76	10	3	13 to 2
2	72 M	116,000	60%	3,900	69%	14	63	6	4	16 „ 0
3	62 F	180,000	50%	5,500	64%	36	74	10	5	11 „ 4
4	44 F	427,000	62%	26,000	80%	43	302	10	10	13 „ 2
5	42 M	299,000	55%	13,050	70%	42	126	10	Discontinued (allergic reaction)	12 „ 4
6	64 M	92,000	93%	12,000	96%	29	192	10	5	12 „ 4
7	59 M	57,000	70%	6,950	73%	14	42	5	4	10 (no effect)
8	34 M	75,000		65,000		42	296	10	Discontinued (no effect)	11 to 9

Previous treatment: Cases 2, 3, 7, and 8 had had myleran; Cases 3, 7, and 8 had also had 6-mercaptopurine.

and 8), colcemid had little effect on the splenomegaly, but these two had also become resistant to "myleran" and 6-mercaptopurine, both of which had failed to influence the degree of splenomegaly. In Case 7, in spite of a reduction in the white-cell count from 57,000 to 6,950 per c.mm., there was no improvement in the clinical condition.

In Table I details of these cases are shown. Cases 2, 3, 7, and 8 had received previous medication with myleran, and Cases 3, 7, and 8 had also had 6-mercaptopurine and had become resistant to treatment; one of these (Case 8) also failed to respond to colcemid. So far, Cases 1–6 have been maintained in satisfactory clinical and haematological states for periods of four to nine months on maintenance doses of 3–10 mg. All were treated as out-patients and carried on with their normal household duties or occupations.

In Case 5, in spite of a very satisfactory remission, colcemid had to be discontinued owing to an allergic reaction, but the patient maintained his improvement after a further three months. At the height of the depressant action on the granulocytes (white cells 11,400 per c.mm.) the patient experienced difficulty in swallowing and had scrotal tenderness and some loss of scalp hair. On examination there was a generalized congestion of the fauces and erythema of the scrotum. This rapidly subsided on discontinuing treatment, and was thought to be a sensitivity reaction to colcemid.

It is important to institute a maintenance dose as soon as the white cells have reached the desired level; failure to do so may result in a rising white-cell count that may be resistant to treatment for several weeks. Fig. 1 shows the effects of instituting a maintenance dose at the correct time, and Fig. 2 shows the effects of withholding an early maintenance dose. It is interesting to note that the second course of colcemid found necessary to restore a normal white-cell count was much greater in total dosage than that required initially—229 mg. as against 63 mg.

In spite of the dramatic effect on the total white cells, in no case did the differential picture return completely to normal. In the majority there was a considerable reduction in the percentage of promyelocytes and myelocytes, but they persisted to a lesser degree when the white cells were restored to a more normal level; in several the initial basophilia persisted.

Marrow biopsies performed after treatment showed reduced cellularity and fewer promyelocytes and myelocytes, but the overall picture still remained that of chronic myeloid leukaemia.

There was a rise in the haemoglobin values and red-cell counts, but their maxima were not reached for several weeks after the white cells had reached their maximal fall. The platelet counts in all were unaffected by the treatment, many remaining at the original high levels.

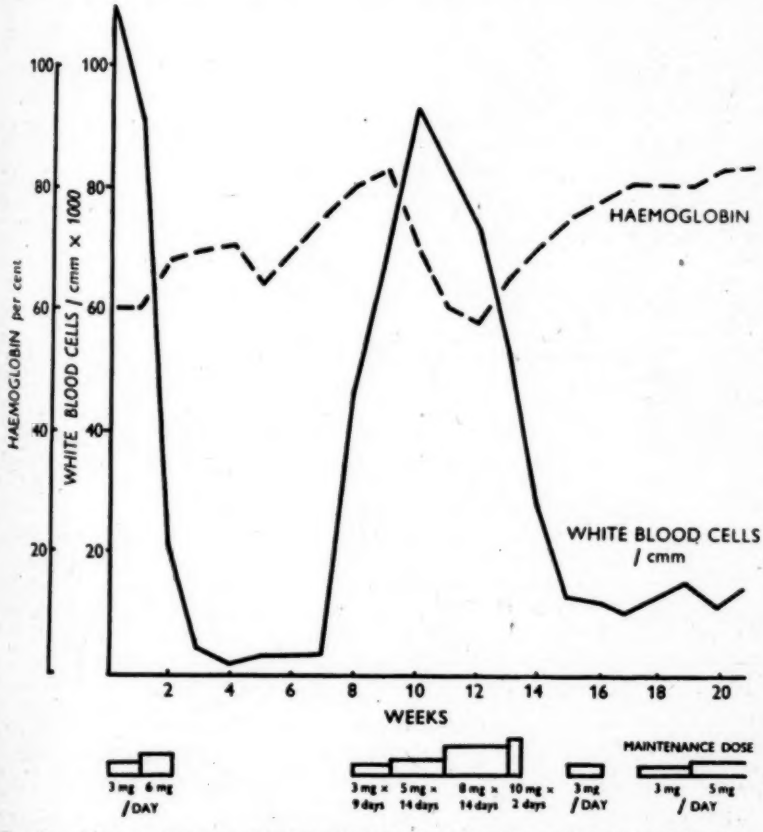

FIG. 2.—Case 2. Effects of colcemid on the total white cells and haemoglobin levels.

Myelofibrosis

The effects of colcemid on two patients with myelofibrosis are shown in Table II. The two cases are described separately because, although presenting like chronic myeloid leukaemia, the clinical and haematological findings suggested that these were actually examples of myelofibrosis.

Case A.—A housewife aged 64, who had had rickets in her childhood, had received *x*-ray treatment for chronic myeloid leukaemia before she was referred to us; attempts to obtain a marrow specimen had been repeatedly unsuccessful. Five months after *x*-ray treatment she was admitted to hospital complaining of severe bone pains in the limbs, loss of energy, and dyspnoea. The spleen was enlarged 13 cm. below the subcostal margin; red cell count, 3,320,000 per c.mm.; haemoglobin, 60%; platelets, 130,000 per c.mm.; total leucocyte count, 56,400 per c.mm. (polymorphs 4.5%, lymphocytes 2%, monocytes 0.5%, eosinophils 0.5%, basophils 0.5%, "blasts" 3%, promyelocytes 3.5%, myelocytes 11.5%, metamyelocytes 3%, atypical cells 71%). The atypical cells resembled normoblasts but were found to be peroxidase-positive. Attempts to obtain marrow from the sternum and iliac crest were repeatedly

TABLE II.—*Myelofibrosis Treated with Colcemid*

Case	Age and Sex	Before Treatment		After Treatment		Duration of Initial Treatment (Days)	Total Dose (mg.)	Maintenance Dose (mg.)	Effects on Splenomegaly (cm. Below Costal Margin)
		W.B.C.	Hb	W.B.C.	Hb				
A	64 F	56,400	60%	7,200	56%	3	3	1	13 to 8
B	40 F	75,000	62%	26,100	56%	5	15	2–3	15 „ 12

unsuccessful: the bones were found to be extremely hard, but *x*-ray films of the skeleton showed no detectable abnormality.

Colcemid was administered cautiously in a dose of 1 mg. daily, and after a total dosage of 3 mg. the white cells were 7,200 per c.mm., red cells 3,010,000 per c.mm., haemoglobin 54%, and platelets 125,000 per c.mm. The differential count showed a persistence of the atypical granulocytes: polymorphs 5.5%, lymphocytes 1%, monocytes 0.5%, eosinophils 1%, basophils 0.5%, "blasts" 2%, promyelocytes 2%, myelocytes 9%, atypical cells 78.5%. Transfusions were given and the haemoglobin eventually rose to 81%, and the loss of energy and dyspnoea subsided. The bone pains were controlled with phenylbutazone 200 mg. twice daily. She has been maintained in this improved clinical state for six months on a daily dose of colcemid 1 mg. The white-cell count has been kept within normal limits, but the abnormal differential has remained more or less unchanged.

Case B.—A housewife aged 40 was referred to us with a history of sudden haemoptyses and was found to have anaemia and considerable splenomegaly (15 cm. below the subcostal margin). A blood count showed: red cells, 4,550,000 per c.mm.; haemoglobin, 62%; platelets, 305,000 per c.mm.; white cells, 75,000 per c.mm. (polymorphs 54%, lymphocytes 11%, eosinophils 3.5%, basophils 4%, myeloblasts 13.5%, promyelocytes 1.5%, myelocytes 8%, metamyelocytes 4.5%); there were 6 nucleated red cells per 200 white cells. The marrow biopsies in several different bones were repeatedly unsuccessful; with the use of considerable force the needle entered the marrow cavity, but no marrow was ever aspirated. Radiological examination of the skeleton and chest was negative. After a total dosage of 15 mg. of colcemid, the white-cell count fell to 26,100 in five days (polymorphs 31.5%, lymphocytes 8.5%, monocytes 0.5%, eosinophils 3%, basophils 17.5%, "blasts" 14%, promyelocytes 4%, myelocytes 14%, metamyelocytes 7%); haemoglobin, 56%; red cells, 4,540,000 per c.mm.; platelets, 300,000 per c.mm. The patient felt improved in herself, had far more energy, and there were no further bleeding episodes. On a daily maintenance dose of 2–3 mg. this clinical improvement has been maintained for five months, the total white cell count has been kept within normal limits, but the abnormal differential count has remained unchanged.

Chronic Lymphatic Leukaemia

Case X.—A man aged 63 presented with generalized lymphadenopathy, splenomegaly (5 cm. below costal margin), and blood and marrow pictures of chronic lymphatic anaemia. The blood picture before treatment was red cells, 3,670,000 per c.mm.; haemoglobin, 83%, white cells, 224,000 per c.mm. (polymorphs 5%, lymphocytes 91%, lymphoblasts 3%, metamyelocytes 1%).

Colcemid, 3 mg., was given daily, and after six days' treatment the white cells had risen to 326,000 per c.mm., while the differential count showed 17% lymphoblasts. His general condition deteriorated with pyrexia, anorexia, and malaise. Treatment was discontinued and within seven days the "blasts" disappeared from the peripheral blood and the white-cell count dropped to its initial level, while his clinical condition slowly improved.

There is no doubt that colcemid aggravated the condition, and if treatment had not been discontinued an irreversible acute leukaemic phase might well have persisted. This experience is similar to that of Moeschlin *et al.* (1953), and we feel that colcemid should not be given to patients with lymphatic leukaemia.

Acute Myeloid Leukaemia

In Table III Cases I, II, and III had acute myeloblastic leukaemia which had failed to respond to other forms of therapy, and Case IV had received no previous treatment. Cases V and VI had suffered from long-standing chronic myeloid leukaemia which had developed an acute myeloblastic phase.

Colcemid was given in doses of 3 mg. daily and increased to a maximum of 5 mg. a day, while supportive therapy with transfusions and antibiotics was also given.

Colcemid had little effect on the clinical condition in Cases I–III; there was no improvement in general well-being and no effect on the bleeding diathesis. However, in all there

TABLE III.—*Acute Myeloid Leukaemia Treated with Colcemid*

Case No.	Before Treatment		After Treatment		Time taken (Days) for Blood Changes in the Previous Column	Previous Treatment	Duration of Leukaemia from Start of Treatment and Present Clinical Condition
	W.B.C.	"Blast" Cells	W.B.C.	"Blast" Cells			
I	37,100	95%	26,000	49%	14	6-Mercaptopurine. Cortisone	Died 3 months
II	18,100	13%	7,400	30%	17	A.C.T.H. gel	„ 3 „
III	24,000	54%	7,950	32%	27	„	„ 5 „
IV	9,200	69%	2,400	19%	14	None	„ 3 „
V	148,000	38%	253,000	32%	31	Myleran. 6-Mercaptopurine	Still living 4 months. Very poor condition
VI	57,000	42%	90,000	32%	21	Myleran	Still living 5 months. Very poor condition

was a fall in the total white-cell counts and a decrease in the number of myeloblasts. The red cells and platelets were reduced in numbers, and this would probably have been more pronounced had transfusions not been given.

Colcemid did not have any beneficial effect in Cases V and VI; in fact, their white-cell counts increased and their clinical condition deteriorated.

Discussion

The results of treating chronic myeloid leukaemia with colcemid are encouraging. It appears that this compound is a more selective granulocyte depressant than other chemotherapeutic agents. The disadvantage of myleran in producing thrombocytopenia and aplastic anaemia, and in some cases precipitating an acute myeloblastic leukaemia, have so far not been seen in any of this small group of cases after treatment with colcemid. This drug is more effective in the early stages of chronic myeloid leukaemia, but in one patient who had survived for four years (on a variety of chemotherapeutic agents) it was completely ineffective. The clinical effects are just as striking as the effects on the blood; with reduction of splenomegaly, improvement in appetite and increase in weight and general well-being were very notable features. From the early results with colcemid it would appear worthy of further trial in chronic myeloid leukaemia, so that its long-term effects may be compared with other well-tried forms of therapy.

In both the patients with myelofibrosis the white cells were extremely sensitive to colcemid and dropped to low levels in three and five days respectively. This is in sharp contrast to the effects on the white cells in the more typical chronic cases of myeloid leukaemias.

The results of treating acute myeloid leukaemia and the acute phase of chronic myeloid leukaemia were disappointing. In spite of some reduction in the number of myeloblasts in the differential counts clinical deterioration continued, and in no case was a complete or even temporary remission obtained.

Summary

The effects of desacetylmethylcolchicine ("colcemid") on some cases of chronic myeloid leukaemia, myelofibrosis, chronic lymphatic leukaemia, and acute myeloblastic leukaemia are described.

Colcemid is of greatest value in chronic myeloid leukaemia, having a distinct depressant action on the

granulocytes and producing rapid reduction of splenomegaly and a marked clinical improvement in six of eight such treated cases.

The disadvantage of many other agents such as myleran in producing thrombocytopenia and aplastic anaemia was not seen in cases of chronic myeloid leukaemia treated with colcemid.

The effects of colcemid on myelofibrosis are considered.

Colcemid would seem to be contraindicated in the treatment of chronic lymphatic leukaemia, and evidence suggests that it may even produce an acute change.

Colcemid has little or no beneficial effects on acute myeloblastic leukaemia.

This work has been done during the tenure by one of us (B. J. L.) of the Sybil Mary Pilkington Research Fellowship, and we would thank Messrs. Ciba Ltd. for the supply of colcemid.

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TEN-YEAR RECOVERY FROM CHRONIC LYMPHOCYTIC LEUKAEMIA

BY

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Reports of recovery from leukaemia are extremely rare. I wish to present the case of a patient who undoubtedly suffered from chronic lymphocytic leukaemia eleven years ago, but has since recovered both clinically and haematologically and has so far survived for ten years. I wish to stress that the point here is not the time of survival. Many patients have survived for ten and more years, but they have always shown signs of the disease, at least as far as an abnormal blood picture.

Case Report

The patient, a female textile worker, was born in 1882. In April, 1940, she had a severe attack of faucial diphtheria with pharyngeal palsy, diaphragmatic palsy, head-drop, and brachial palsy. There was nothing else relevant in her past history.

When seen on July 7, 1943, she complained of lassitude, dyspnoea, sweating, cramps in the legs, and indigestion for about one year. For the same period she had had two lumps in the left armpit.

Examination showed enlarged cervical, supraclavicular, axillary, and inguinal lymph nodes. They were firm, discrete, and quite painless. The spleen extended as far as the left iliac fossa, the notched medial border reaching the umbilicus. It was not tender. The sternum and tibiae were tender on tapping. There were some bluish nodules under the nail-bed of some toes. The urine showed a trace of albumin. There was no excess of urobilinogen or urobilin, and nothing abnormal in the deposit. Blood: R.B.C., 3,480,000; Hb, 70%; C.I., 1; W.B.C., 224,000 (polymorphs 3,360, lymphocytes 219,520, monocytes 1,120). The lymphocytes were fairly mature cells bigger than normal. The stain was taken well by the red cells. There were no nucleated red cells.

The patient was admitted for *x*-ray therapy, eight doses of 50 r each being given to the spleen. Thereafter the margin of the spleen was just palpable below the ribs, and the W.B.C. numbered 17,100, with 13,766 lymphocytes.

She began to lose her tiredness, dyspnoea, and abdominal pain, and started to feel well. The lymph nodes became gradually smaller, without, however, returning to normal size. The spleen was firm and painless and remained palpable three fingerbreadths below the left costal arch. Serial blood counts (see Table I) showed normal haemoglobin and red cells, with slightly raised total leucocytes, of which 75–80% were lymphocytes.

It was decided to give a further series of *x* rays to the cervical and axillary glands, and 50 r to four fields twice weekly to a total of 400 r was applied in May, 1944. Thereafter the glands were smaller, soft, discrete, freely mobile, painless, and about the size of a pea. The inguinal glands were no longer palpable. The size of the spleen was unchanged. The patient felt well in herself and did her housework and shopping.

In February, 1945, she developed a lower respiratory infection, the first of many more to follow. She made a slow recovery on symptomatic treatment, the blood picture being unchanged. After this the margin of the spleen could only just be felt below the ribs. The glands were unchanged in size. Further serial blood counts throughout 1945 and 1946 were normal (see Table I). In January, 1947, she again developed bronchopneumonia. In April the blood picture returned to normal. Cervical and axillary glands were palpable, and the spleen could not be felt. At the end of June, 1947, she again developed bronchitis, and a further bronchopneumonic attack occurred in December, 1947, and again in June, 1948. No glands could be felt anywhere, nor was the spleen palpable in December, 1948. In March, 1949, she started once more to cough and was feverish. She again had pneumonia in April, 1950, in January, 1951, and in April, 1952. She had a *Haemophilus influenzae* infection in January, 1953. In January, 1954, she developed erysipelas of the right cheek and forehead.

A blood count in July, 1954, revealed a hypochromic anaemia (Hb 65%). Seven weeks later, after iron medication, the haemoglobin was 83%.

Cases from the Literature

It is difficult to find sufficiently well-documented cases in the literature for comparison. Forkner (1938) quotes quite a number of cases, but most of these do not bear close scrutiny. Naegeli (1931), referring to chronic lymphocytic leukaemia, states that "published cures relate probably always to lymphatic reactions." Heilmeyer and Begemann (1951) in the latest German textbook do not even mention cure. Kolmer (1949) states that true leukaemia is invariably fatal, alleged recovery being due to errors in diagnosis. Wintrobe (1951) merely states that there are a number of reports of cure, but does not give his own opinion. So much for the rarity, even denial, of the possibility of recovery.

One case of recovery was described by Schiassi (1933).

A man aged 20 developed right pleurisy in 1911. In 1923 he developed left pleurisy with fluid. An enlarged spleen was found. A blood count in 1924 showed 200,000 leucocytes, of which 40% were immature granulocytes. Chronic myelocytic leukaemia was then diagnosed and a series of *x*-ray treatments were given. On his discharge in December, 1924, the leucocytes numbered 25,200, with 10% immature granulocytes. The spleen and liver were reduced to nearly normal limits. He returned to work. In July, 1928, he suffered from lassitude, loss of appetite, and pains in the right leg. He had 120,000 leucocytes (12% immature). Further *x*-ray therapy was given and the leucocytes fell to 12,400 on discharge. In December, 1931, he again felt weak and had pain in the left hypochondrium. The spleen and liver were not palpable. He had 18,740 leucocytes, with some myelocytes. In February, 1933, he had a haemoptysis. There were no palpable lymph nodes anywhere. The liver and spleen could not be felt. There was diminished air entry over the left lower chest and an *x*-ray film showed pleural thickening at the left base. The lung

TABLE I

Date	Hb %	R.B.C. (mil./c.mm.)	C.I.	Leucocytes	Polymorphs	Lymphocytes	Monocytes	Eosinophils	Basophils
				per c.mm.					
7/7/43	70	3·48	1·00	224,000	3,360	219,520	1,120	0	0
6/8/43*	75			41,400	4,554	36,432	414	0	0
13/8/43	62			17,150	2,658	13,806	600	86	0
17/8/43	62			17,100	2,650	13,766	684	0	0
29/9/43	89	5·35	0·83	9,900	1,881	7,920	0	99	0
7/12/43	97	4·44	1·09	9,100	1,729	7,189	91	21	0
8/2/44	86	4·81	0·89	10,900	2,289	8,284	327	0	0
18/4/44	95	4·54	1·05	11,200	2,016	8,848	112	112	112
31/5/44*	80	4·03	1·00	12,800	3,072	9,088	512	128	0
25/7/44	83	4·45	0·93	8,600	1,806	6,622	172	0	0
18/10/44	91	5·16	0·88	6,200	2,232	3,782	124	62	0
24/1/45	85	4·87	0·85	8,000	2,480	5,120	80	160	160
15/2/45†				3,800	1,786	1,938	76	0	0
24/4/45	93	4·94	0·94	7,200	2,160	4,896	0	0	144
7/8/45	105	5·34	0·98	5,000	2,200	2,700	0	50	50
6/11/45	89	5·15	0·86	4,900	1,568	3,185	147	0	0
7/5/46	87	4·91	0·89	3,300	2,079	1,089	132	0	0
6/8/46‡	77	4·39	0·88	2,800	1,484	1,036	168	84	28
4/1/47§	83	3·90	1·05	16,100	11,753	2,737	966	483	161
19/1/47§	73	3·83	0·95	11,100	8,325	1,443	666	666	0
28/4/47	85	4·49	0·95	7,900	4,503	2,528	632	237	0
18/8/47	80	4·64	0·86	1,525	320	1,159	31	15	0
19/9/47	84	4·59	0·92	5,000	3,100	1,550	100	200	50
8/3/48	93	4·54	1·02	2,600	1,820	624	78	52	26
6/8/48	90	4·81	0·94	7,000	4,690	2,030	140	140	0
29/12/48	89	4·36	1·02	5,700	3,591	1,710	228	114	57
5/8/49	84	5·02	0·84	5,300	3,816	1,219	212	53	0
9/1/50	87	5·02	0·87	4,500	3,060	1,215	225	0	0
7/8/50	97	4·26	1·14	4,000	3,000	960	40	0	0
27/6/51	82	4·68	0·88	7,300	4,307	2,774	146	73	0
25/7/52	85	4·73	0·9	5,000	2,800	1,750	250	150	50
14/7/53	92	4·61	1·0	3,200	2,080	864	64	160	32
21/6/54	65	5·53	0·59	6,800	4,352	2,108	272	0	68
11/8/54	83	4·90	0·85	3,900	2,652	1,092	117	39	0

* After *x*-ray therapy. † "Cold." Temperature 101° F. (38·3° C.), pulse 80. ‡ "Cold." § Pneumonia.

TABLE II (*Modified from Schiassi*, 1933)

Date	Hb %	R.B.C. (mil./c.mm.)	Colour-index	Leucocytes	Myeloblasts and Promyelocytes	Myelocytes	Metamyelocytes	Polymorphs	Eosinophils	Basophils	Lymphocytes	Monocytes
				per c.mm.								
9/8/24	85	4·160	1·0	200,000	26,800	34,000	13,800	115,600	1,600	0	5,000	3,200
28/8/24	45	4·500	0·5	275,000								
5/9/24	First *x*-ray treatment											
9/10/24	54	3·800	0·71	152,800	13,752	10,696	22,920	79,456	7,640	1,528	10,696	6,112
31/10/24	Second *x*-ray treatment											
	60	3·800	0·79	82,000								
1/12/24		4·750		25,200	504	630	1,764	17,388	756	252	2,142	1,764
18/7/28	54	4·900	0·55	120,000	6,000	8,400	0	102,000	1,800	0	600	1,200
24/7/28	Third *x*-ray treatment											
25/7/28	Fourth " "											
23/7/28	Fifth " "											
27/8/28	47	3·800	0·61	12,400								
8/1/32		4·108		18,740	Some myelocytes and promyelocytes			14,992	187	187	2,624	562
19/5/32	90	4·900	0·91	7,000				5,915	175		665	245
8/3/33	60	3·725	0·81	7,400				6,038	222	45	414	618
7/5/33	80	4·600	0·87	5,100				3,825	102	26	867	280

fields were otherwise clear. No tubercle bacilli were found in the sputum. The blood (see Table II) showed a slight hypochromic anaemia. The number of leucocytes was normal. The differential count was normal except for an increased percentage of neutrophils and a decrease of lymphocytes.

Another case was reported by Gloor (1930) from Naegeli's clinic, but was followed up for only two years.

Discussion

The case of chronic myelocytic leukaemia reported by Schiassi seems the only one comparable to the case reported here. I have quoted it more extensively because I think it is not as well known as it deserves to be, possibly owing to the fact that it was published in a little-known journal. Schiassi himself concludes that one can no longer talk of leukaemia or a leukaemic myelosis, but that it is now a case of a chronic respiratory affection with slight hypochromic anaemia. The fact remains that his case shows five years' remission with clinical and haematological recovery.

With regard to the case now reported, I do not think that the diagnosis of chronic lymphocytic leukaemia is in doubt at all. The clinical findings, enlarged lymph nodes, and enlarged spleen, together with the blood picture of moderate orthochromic anaemia and 219,520 lymphocytes, represent a classical case.

The patient has twice been subjected to *x*-ray therapy. There was a steady decline in the number of lymphocytes after the first course, and after the second course the blood picture became normal and has remained so. It would be impossible now to make a diagnosis of chronic lymphocytic leukaemia from the blood picture. The spleen and lymph nodes were a little slower in regressing, but the spleen has been impalpable since April, 1947, and the lymph nodes since August, 1948. A remarkable feature of this patient is her proneness to infections, almost wholly respiratory. It is not clear whether this is due to leukaemia or whether she has a diminished resistance, or whatever one likes to call it. It must be pointed out, however, that she did not suffer from these infections before she had leukaemia.

There is a voluminous literature covering the influence of infections on leukaemia. As regards the effect of infections, Jaffé (1932) found the normal defence reaction lacking in the absence of myeloid tissue. Wintrobe (1951) states that this is consistent with his findings of a higher incidence of infections in cases of lymphocytic as compared with myelocytic leukaemia, and an unusual vulnerability to infections in the former. My patient with chronic lymphocytic leukaemia seemed certainly more vulnerable to infections. However, as her blood picture has been normal for the past ten years it must be assumed that she possessed a normal amount

of myeloid tissue, sufficient for a normal defence reaction. Her proneness to infections cannot therefore be explained by a lack of myeloid tissue. If one assumes that it has some connexion with the leukaemia one has to look for another explanation. It may be that the formation of antibodies was altered in some way, if it is assumed that these are formed by lymphocytes. However, this is unproved. Hickling and Sutliffe (1928) report a case of pneumonia in chronic lymphocytic leukaemia in which they found a moderate amount of protective antibodies in the serum after recovery.

The question of a remission of leukaemic signs through intercurrent infections has been summed up by Wintrobe and Hasenbush (1939). They come to the conclusion that there is little evidence for this even in the literature. In the case here presented it does not seem that the frequent infections have contributed to the remission. The recovery has taken place throughout unaffected by the infections.

Summary

A case is presented of ten years' clinical and haematological recovery from chronic lymphocytic leukaemia.

The clinical history of the patient, with blood pictures extending over eleven years, is given.

The literature is reviewed and one similar and one doubtful case are quoted and discussed.

The present case is discussed as regards diagnosis, frequency of intercurrent infections, and the influence of infection on leukaemia.

It is a great pleasure to thank Dr. C. J. Young, head of the Pathological Department, Bradford Royal Infirmary, for his constant encouragement, without which this paper would not have been written, and for kindly going through the manuscript. He has also given me considerable help with the laboratory investigations and advice in the management of the patient. I also wish to thank Dr. F. E. Chester-Williams for treating the patient and for permission to quote details of the *x*-ray treatment.

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The number of fatal accidents in the home is rising every year, according to the figures quoted by C. A. Boucher in the March issue of the *Monthly Bulletin of the Ministry of Health*. Whereas there were 4,904 fatal accidents in 1949, in 1953 there were 5,895. During the last ten years 57,413 people have died as a result of home accidents, and of these approximately 10,000 were children aged under 5; children under 5 and old people of over 65 accounted for four-fifths of the total figure, the peak risk period for a child being in the third year of life. Although 1953 saw a drop in the figures of children killed accidentally, the number of old people affected increased, about 60% of the accidents in this group being due to falls. It was hoped that the regulations introduced under the Heating Appliances (Fireguards) Act of 1952 would reduce the fatalities due to burns, but the provisional figures for 1954 indicate that the situation has worsened. The regulations apply only to heating appliances on sale and not to those already in the home. To counteract the large number of these fatal accidents the Home Safety Department of the Royal Society for the Prevention of Accidents has set up 70 local committees and hopes to set up more. A Home Safety Group has also been inaugurated, which will supply posters and propaganda.

USES OF CHLORPROMAZINE IN MENTAL HOSPITAL PATIENTS

BY

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Since its original use by Laborit and Huguenard (1951) in anaesthetic practice chlorpromazine hydrochloride ("largactil") has found a steadily increasing application first in the anaesthetic sphere and later in psychiatry.

Courvoisier *et al.* (1953) have investigated the pharmacology of the drug in animals, and from the psychiatric standpoint its most important properties appear to be its depressant effect on central nervous and autonomic activity and its potentiation of narcotic and analgesic drugs.

Early investigation into the psychiatric uses of the drug by Delay and his collaborators, reported in a series of papers (see References), has subsequently been confirmed and enlarged upon by a number of workers on the Continent, particularly by Sigwald and Bouttier (1953a, 1953b), Staehelin and Kielholz (1953), Flügel (1953a), and more recently in this country by Anton-Stephens (1954). All authors are agreed that its most striking effect is its sedative action in all states of tension, agitation, or excitement of whatever origin, but that this sedative effect is entirely different from that produced by the barbiturates or other hypnotics in that the patient is able to take a normal interest in his environment and perform his ordinary duties without, except in the early stages, any undue sleepiness.

Even when a soporific state arises, the patient is as easily roused as from normal sleep and tends to fall asleep only if he has no external interests at the time. Furthermore, Flügel (1953b) has shown that there is no falling off in mental capacity as measured by psychological tests—in some cases there is even an increase—and that the E.E.G. is not altered in the same way as with ordinary hypnotics. This unique sedative action of the drug has been variously described as a "chemical leucotomy" (Delay and Deniker), "a harmonizing of the personality" (Flügel), and "a state of psychic indifference (Anton-Stephens).

The drug has been used in a wide variety of psychiatric conditions, and some success has been reported in almost all these conditions, but the most generally accepted indications are excitements of all kinds (manic, schizophrenic, or organic), agitated depression, neurotic tension states, and drug intoxications. Opinion about its effect on chronic psychotic states is more divided, but these conditions have been less extensively investigated.

Chlorpromazine has been in use at Springfield Hospital since November, 1953, and between then and the end of July, 1954, just under 500 patients have received the drug for periods varying from a few days to six months.

This paper reports the findings on the 205 patients (55 male and 150 female) who received treatment between November, 1953, and the end of March, 1954.

Selection of Material and Assessment of Results

The earliest cases treated were seriously disturbed chronic psychotics, but as the efficacy of the drug became more apparent the field of application steadily widened to include every type of case catered for by a large mental hospital.

Acute and chronic disturbed psychotics, however, are by far the largest class of patients in the series.

Patients whose treatment had to be stopped for any reason before they had received it for a week, and the few who had E.C.T. concurrently, are excluded from the results, otherwise the series includes all patients starting treatment during the stated period.

Results were assessed either when treatment was stopped or, in cases in which treatment was prolonged, at a time not less than eight weeks after the start.

The following criteria of improvement were used :

1. Not improved.—Slight or no change either in symptoms or in behaviour.

2. Slightly improved.—Decrease in symptoms and disappearance of gross behaviour disturbance.

3. Moderately improved.—Improvement in adjustment at hospital level or to the outside world at a dependent level, as shown by taking an interest in environment and in ward social activities and employability within the hospital.

4. Much improved.—Improved in adjustment to the outside world at an independent level, as shown by increase in initiative, reliability, and responsibility.

5. Recovered.—Symptom-free, with insight and capacity for adjustment to the outside world at the same level extant before the breakdown.

Where there was any doubt about the correct assessment the less favourable was chosen.

Dosage and Management of Cases

The early cases received a commencing daily dosage of 25 mg. t.d.s. intramuscularly, increasing to 50 mg. t.d.s. after the first three days. At the end of a week they were given the same dose orally. Despite reports that the drug is fully and rapidly absorbed from the intestinal tract, it was soon realized that a larger oral dose was required to produce the same effect. The oral dose was therefore increased to 75 mg. t.d.s. Later the intramuscular route was abandoned except in those who were too resistive to take drugs readily by mouth, as there seemed no special advantage in starting treatment by injection. This, however, is contrary to the findings of most other workers, who advocate starting treatment by injection except in very mild cases. Subsequent attempts to confirm the finding that treatment is more effectively initiated by intramuscular injection have failed to reveal any advantage. Improvement when it occurred was gradual whether the drug was administered orally or by injection, and the dramatic effects produced in the first 24 hours that are quoted by most authors were absent in this series.

Although there were many individual variations, the most generally adopted scheme of dosage in the later cases was to give 50 mg. t.d.s. orally in the first week, 75 mg. t.d.s. in the second week, and 100 mg. t.d.s. in the third and subsequent weeks. Very few patients failed to tolerate this dosage, and these were mainly among the neurotics and mildly disturbed psychotics.

Some patients received higher dosages than 300 mg. daily, but in general the impression gained was that most patients who improved with the drug did so on 150 mg. daily. Of those who failed to improve on 150 mg. a large number improved when the dose was increased to 225 mg. daily, and of those who still failed to improve at this level a few did so on 300 mg. Little further improvement could be expected with higher doses.

The more disturbed and chronic psychotic patients both tolerated higher dosages and required more drug to produce betterment. Improvement was noticed in some cases within a few days of starting treatment but in others not for several weeks. In only one case did improvement start after the patient had been on treatment for more than two months, and in the great majority of cases the maximum benefits of the drug had been achieved in three months. Treatment was therefore not abandoned as useless in under two months and was not as a rule prolonged beyond three. It was terminated abruptly without any withdrawal effects being noticed in any case.

Almost all cases treated were ambulant from the start, the only exceptions being those whose mental state necessitated a period in bed, and all elderly people or those with cardiovascular dysfunction. Although a few patients complained of slight giddiness, particularly during the first few days of treatment or immediately following an increase in dosage, no marked hypotensive effects were observed except in those with arteriosclerosis or some other cardiovascular disease and in one other case.

In the early cases all sedatives were withdrawn and only later prescribed with great caution owing to the possible risk of potentiation. Experience, however, showed that this risk was negligible in normal dosage, most patients not only tolerating but also at first requiring whatever sedatives they had been having before the start of chlorpromazine treatment. The potentiating effect of chlorpromazine was noticeable only in those in whom continual narcosis was produced, when it was possible to do so with much smaller doses of barbiturates in association with chlorpromazine than would have been possible with barbiturates alone.

Unless, therefore, individual needs suggested some modification, it was customary to treat ambulant patients with an initial dosage of 150 mg. daily ; to increase this to 300 mg. in the course of three weeks ; and to maintain it at this level for three months, when treatment was abruptly terminated. But as opinion about the most suitable dosage and duration of treatment was changing throughout the period under review there is no doubt it will continue to evolve in the light of further experience.

Results

Table I shows the results in the different diagnostic groups in 196 cases. The remaining nine patients died while under treatment. They were all elderly patients and seriously ill physically before chlorpromazine was started. None were expected to live. The cause of death, which was in each case ascertained by post-mortem examination, was pulmonary embolus from femoral thrombosis in one case, and in the rest either bronchopneumonia or the cardiovascular changes associated with senility. It was not thought that chlorpromazine could in any way be incriminated.

TABLE I.—*Results in Different Diagnostic Groups*

Diagnosis	Recovered		Much Improved		Moderately Improved		Slightly Improved		Not Improved		Total No. of Cases
	No.	%	No.	%	No.	%	No.	%	No.	%	
Schizophrenic group of diseases	4	3	17	12	39	29	39	29	37	27	136
Endogenous depression ..	2	11	4	21	4	21	2	11	7	37	19
Neuroses and psychopathic states	2	11	6	33	2	11	1	6	7	39	18
Organic states ..	—	—	—	—	6	38	5	31	5	31	16
Mania and hypomania	1	14	—	—	2	29	2	29	2	29	7
Total ..	9	5	27	14	53	27	49	25	58	29	196

Schizophrenics comprise the largest single group, and a sufficient number have been treated to form a rather more definite impression of the value of the drug than in any other diagnostic group. But although 136 cases have been treated, no very definite prognostic criteria have emerged, both remarkable successes and equally unexpected failures being quite common. In the more acutely disturbed patients, the drug has a quieting effect in a few days, but the dramatic change described by other authors within 24 hours has not been noticeable in this series. In fact, where excitement has been intense it has invariably been necessary to give barbiturates in large doses in addition to chlorpromazine. It is, however, in just these acutely disturbed patients that the prognosis in schizophrenia is best, and it is doubtful whether chlorpromazine in any way improves

the outlook, although it is certainly a very effective sedative when used either alone or in conjunction with barbiturates.

On the other hand, in schizophrenics of poor prognosis—that is, in chronic cases and in the paranoid group—the value of the drug is much less ambiguous. Of the 136 schizophrenics treated, 55 had been in hospital continuously for two years or longer; their average age was 41 ± 1.8 years and the average stay in hospital prior to treatment 8.5 ± 0.9 years. All of them were seriously disturbed patients, but in this extremely unpromising group the following results were obtained: much improved, 2 (4%); moderately improved, 15 (27%); slightly improved, 21 (38%); not improved, 17 (31%).

The two patients who were much improved had both been in hospital for four years and both had previously had insulin, E.C.T., and prefrontal leucotomy without any improvement at all. They were both very difficult turbulent patients. One of them has now been out of hospital for three months and is earning her living, and the other is expecting to leave shortly.

The effect of the drug in these cases is somewhat similar to that of leucotomy but without its disadvantages. There is first a stage which Anton-Stephens well describes as one of psychic indifference in which delusions and hallucinations persist but no longer have the same emotional significance, and consequently there is considerable improvement in behaviour. Later the delusions and hallucinations themselves fade and in some few patients an unexpected degree of insight has developed.

In some patients the effects are clearly symptomatic only, as relapse occurred shortly after withdrawing the drug. But, although the long-term results of chlorpromazine treatment are as yet unknown, immediate relapse is surprisingly rare even in chronic patients if the drug is not withdrawn too soon. And improvement, once started, often continues for many weeks after the drug has been discontinued. It is felt, therefore, that an important effect of chlorpromazine is to make possible the rehabilitation of patients who were formerly too disturbed for this to be accomplished. In this respect it can again be compared to leucotomy.

In endogenous depression the results shown in Table I are unimpressive. This can largely be attributed to the fact that patients who failed to respond quickly to chlorpromazine were taken off the drug and given E.C.T. It is therefore possible that if treatment had been prolonged results would have been better. In general it was felt that E.C.T. is a more effective treatment for depression than chlorpromazine. On the other hand, in two cases of chronic retarded depression of nearly two years' duration which had either failed to respond or had responded but briefly to E.C.T., given on more than one occasion in the past, the results were excellent, a far more satisfactory remission being achieved with chlorpromazine, and one which has so far lasted in the first instance for four months, and in the second for two. Chlorpromazine may therefore prove a useful line of treatment in cases of depression which fail to respond to E.C.T.

In the 16 patients suffering from organic dementia improvement was largely symptomatic and relapse was frequent when treatment was stopped.

The findings in neurotic patients were in agreement with those of other workers in suggesting that states of anxiety or emotional tension were the most likely to respond to chlorpromazine. On the other hand, one chronic hysteric, whose principal complaint was irritation of the ear, completely lost her symptom. That this was a direct response to chlorpromazine and not due to suggestion was demonstrated by substituting identical neutral tablets, unknown to the patient, when her symptoms returned, to disappear once more when chlorpromazine treatment was resumed.

Psychopathic states behaved in a similar way to neuroses, the best results occurring when there was considerable associated anxiety. In one class of patients, the aggressive psychopaths, chlorpromazine appeared definitely to be contraindicated. Not only did it not produce any improvement, but it often increased the tendency to explosive outbursts of violence. While the number of cases in the series is too few to be more than suggestive, this experience has been repeated in cases treated subsequently.

Of the seven cases of mania and hypomania treated, only one was better than moderately improved. This man, who recovered, was the only case of acute manic excitement treated, and the effect of chlorpromazine was very impressive. Barbiturates had controlled his excitement only very ineffectively and he had developed pneumonia, so that both his physical and his mental conditions were causing grave concern. Within 48 hours of starting chlorpromazine he was overactive and euphoric, but was co-operating well and was no longer a nursing problem of any sort. The other six cases were all chronic hypomanics, and a good hospital adjustment was the best that could be achieved.

All patients were classified as acute, subacute, or chronic cases, according to the time they had been in hospital before treatment was started. Those who had been in less than six months were regarded as acute cases, from six months to two years as subacute, and over two years as chronic. This method of classification has the merit of being unambiguous. On the other hand, it does not take into account previous breakdowns, or the duration of the illness prior to admission. As information on this score was too often missing, it was felt to be the most satisfactory classification in the circumstances, but it is obviously biased towards the acute end of the scale.

In general, most of the acute cases were receiving chlorpromazine as the first line of treatment, the subacute group had recently failed to respond to some other form of therapy, and the chronic group had already received all appropriate treatment for their condition without improvement. There was no difference in the average age of the three groups, which was just over 40, nor in the dosage they received, and the mean durations of illness were 6 weeks, 13 months, and 9 years respectively.

Table II shows the results.

TABLE II.—*Results Analysed According to Duration of Stay in Hospital Before Treatment*

Time in Hospital Before Treatment	Recovered		Much Improved		Moderately Improved		Slightly Improved		Not Improved		Total No. of Cases
	No.	%	No.	%	No.	%	No.	%	No.	%	
1–6 months ..	9	10	20	21	23	25	19	20	22	24	93
6–24 ,, ..	—	—	5	13	15	39	6	16	12	32	38
Over 2 years ..	—	—	2	3	15	23	24	37	24	37	65
Total ..	9	5	27	14	53	27	49	25	58	29	196

As might be expected, the best results were achieved in the acute cases. But there are too many imponderables concerned in assessing the results in acute psychiatric cases for any definite assertions to be made about a new line of treatment unless carefully controlled trials are made, and this the present survey does not pretend to be. The preliminary impression gained is that chlorpromazine has a part to play in the treatment of acute psychiatric conditions of all sorts, but the detailed indications for its use remain to be worked out. In the subacute group, the part played by extraneous factors in any improvement produced becomes less important, and in the chronic cases any change can even more certainly be attributed to the drug. It is in these two groups that the value of chlorpromazine is felt to be beyond doubt.

It will be noted that 37 out of the 103 subacute and chronic patients (36%) reached a level of good hospital adjustment or better. All the patients in these two groups were previously making a poor adjustment and the great majority were seriously disturbed.

The indications for chlorpromazine have been considered by most authorities to be largely symptomatic—that is, in

states of excitement, agitation, or emotional tension. All patients were classified, therefore, according to their psychomotor state. In the overactive group were classed excited, aggressive, or emotionally unstable schizophrenics, manics, agitated depressives and seniles, and anxious neurotics, while the inhibited group contained catatonic stupors and detached schizophrenics, retarded depressives, and apathetic neurotics. Detached schizophrenics who became periodically impulsive were placed in a separate category.

The results shown in Table III are somewhat surprising. Although more patients recovered in the overactive group and more inhibited patients did not improve, if the recovered

TABLE III.—*Results Analysed According to Psychomotor State*

Psychomotor State	Recovered		Much Improved		Moderately Improved		Slightly Improved		Not Improved		Total No. of Cases
	No.	%	No.	%	No.	%	No.	%	No.	%	
Overactive ..	8	6	17	13	31	25	35	28	35	28	126
Inhibited ..	1	2	9	17	15	29	6	12	21	40	52
Inhibited with impulsive outbursts	—	—	1	6	7	39	8	44	2	11	18
Total ..	9	5	27	14	53	27	49	25	58	29	196

and much improved are grouped together on the one hand and the slightly improved and not improved on the other, the results are almost identical in both inhibited and overactive patients. This suggests that some revision is needed in the conception of chlorpromazine as being mainly a symptomatic treatment for excited states.

Chlorpromazine and Leucotomy

The effects of chlorpromazine have often been compared to those of leucotomy. It might therefore be supposed that patients in whom leucotomy had failed would equally fail to respond to chlorpromazine, and, conversely, that chlorpromazine might prove a useful prognostic indicator for leucotomy. Neither of these suppositions is borne out by the results in this series.

The results in 28 patients in the series who had previously been leucotomized were as follows: much improved, 3 (11%); moderately improved, 6 (21%); slightly improved, 11 (39%); not improved, 8 (29%). These results do not vary significantly from those in the series as a whole, and lend further support to the view that chlorpromazine can be of value in prognostically poor cases.

On the other hand, four patients who failed to respond in any way to chlorpromazine have made a very good immediate response to leucotomy, though it remains to be seen whether this will be maintained.

Side-Effects and Toxic Reactions

The various side-effects and toxic reactions recorded in the literature were noted in this series, but, as their occurrence in a much larger number of cases is the subject of a separate communication, no details are mentioned here.

Summary and Conclusions

The results in 205 patients treated with chlorpromazine are examined.

A tentative scheme of dosage and duration of treatment is discussed. It is not felt that the intramuscular route offers any advantages over the oral.

Results in the different diagnostic categories suggest that chlorpromazine may play a useful part in the treatment of acute states of excitement of all sorts, in neurotics in whom tension or anxiety is a prominent symptom, and in some depressive patients in whom E.C.T. has proved ineffective.

The most striking results, however, were obtained in chronic psychotic patients in whom the prognosis would normally be very bad. It enabled a few of these patients to be discharged and many more to make a good hospital adjustment.

In chronic patients it was felt that the chief part played by chlorpromazine was to make possible the rehabilitation of those in whom this was formerly impossible and that, while in some relapse occurred immediately treatment was stopped, in others improvement still continued.

There seemed to be little difference between its effect on overactive and inhibited patients.

As good results were found after leucotomy as in other chronic patients.

I wish to thank Messrs. May & Baker for kindly making supplies of chlorpromazine available for this trial; Dr. Robert Forgan, of May & Baker, for his very valuable help and advice; and Dr. H. C. Beccle, medical superintendent of Springfield Hospital, for much helpful criticism in the preparation of this paper.

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CHLORPROMAZINE IN TREATMENT OF ELDERLY PSYCHOTIC WOMEN

BY

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One of the difficult nursing problems in a mental hospital concerns the group of elderly long-stay patients who suffer from periods of restlessness, confusion, and disorientation or who are continually in a state of agitation, with stereotyped speech and activity. The Board of Control (1954) stated that, "on January 1, 1953, 28.8% of the mental hospital population were over the age of 65 and two-thirds of these were women."

A related problem is the shortage of nursing staff, owing to which large wards of noisy, difficult patients have to be in the care of too few nurses, or patients have to be left at night with inadequate supervision. It is hoped to show that chlorpromazine ("largactil") may play a part in the solution of these problems.

Since interest in the psychiatric use of chlorpromazine was roused by Sigwald and Bouttier (1953), who summarize the literature, and by Ey and Bérard (1952), who used it as a method of prolonged sleep treatment (*cure de sommeil*) in psychiatric patients, various authors in this country have published series of cases suggesting its value when tension and agitation predominate—Anton-Stephens (1954) on psychiatric patients with varying diagnoses, Garmany *et al.* (1954) in psychoneurosis, Elkes and Elkes (1954) in psychosis, and Howell *et al.* (1954) in geriatrics.

The present series is a group of elderly psychotic women with varying diagnoses but having in common

the fact that they became nursing problems because they were noisy, abusive, violent, and destructive, or required constant attention for feeding and dressing.

Case Material

Forty-eight women aged from 58 to 87 were chosen, all being nursing problems to a varying degree. Many had been in hospital for several years, but some had been recently admitted with diagnoses of senile dementia. Table I shows the age grouping and the diagnoses.

TABLE I.—*Age Grouping and Diagnoses*

Age	No.	Diagnoses	No.
58 ..	1	Schizophrenia (including paranoia paraphrenia)	13
60–70 ..	18	Agitated depression	6
71–80 ..	22	Dementia (all organic causes)	29
Over 80 ..	7		
Total ..	48	Total ..	48

Two of the patients were later withdrawn from the trial —one because she developed jaundice, and the other because she fell and sustained a fractured femur.

Method

These 48 patients were divided into two groups: the parenteral Group P (22 patients), beginning treatment by injection, and the oral Group O (26 patients), receiving oral treatment only.

Group P.—Eleven of these patients were given a course of 50 mg. of chlorpromazine thrice daily by injection for one week, followed by 50 mg. thrice daily by mouth for three weeks. At the same time the other 11 patients received one week's treatment with an equivalent volume of inert control injection followed by three weeks' treatment with inert tablets. At the time of the experiment no one knew into which half of the group each patient fell. At the end of the first four weeks the two half groups were reversed, so that those receiving chlorpromazine now received control tablets while those on control tablets received chlorpromazine. For reasons discussed later, it was felt that patients should not receive further parenteral therapy, and oral therapy alone was used in the second month.

Group O.—This group originally consisted of 26 patients, half of whom began treatment with chlorpromazine, 25 mg. thrice daily for three days, then 50 mg. thrice daily for ten days, and 75 mg. thrice daily for two weeks. It was from this half of the group that the two cases had to be withdrawn. The other half received corresponding numbers of control tablets, and after a month the two halves of the group were reversed in a manner similar to that described above.

Summary of Results

Table II shows the number of patients in each group falling into categories of improvement. Three degrees of improvement were considered:

+ Some improvement: somewhat less agitated and restless; able to sleep without sedative.

++ Definite improvement: more rational and talkative; less restless; not so disturbed by delusions.

+++ Marked improvement: able to look after herself, whereas she had been unable to do so hitherto; spontaneous conversation; could take part in social activities.

Dealing first with Group P, and taking the two treatment subgroups together and the two control subgroups together —that is, A1 and B2, also A2 and B1 (see Table II)—and grouping the results as either improved or not improved, we get $\chi^2 = 17.8$ and $P \leq 0.001$. The difference between the treatment and the control groups was highly significant. Similarly, in Group O $\chi^2 = 16.3$ and $P \leq 0.001$—again highly significant.

TABLE II.—*Number of Patients Falling into Various Categories of Improvement*

	Group P				Group O			
	Improvement			No Change or Relapse	Improvement			No Change or Relapse
	+	++	+++		+	++	+++	
1st month:								
Treatment (A1) ..	4	5	2	0	2	2	3	4
Control (B1) ..	1	0	0	10	3	2	0	8
2nd month:								
Now control (A2) ..	3	0	0	8	2	1	0	8
Now treatment (B2)	2	3	2	4	2	8	2	1

The two patients who were withdrawn were in subgroup A1 of Group O.

It is necessary to differentiate clinically between those patients who improved on treatment and relapsed when receiving control tablets and those who improved when receiving control tablets or in whom no change took place. Combining Groups O and P, patients were found to fall into six further groups (Table III). It will be seen that 28 (60.9%) cases showed some degree of improvement with chlorpromazine, while if group 3 is added the figure is 33 (71.7%).

TABLE III.—*Number of Patients in Each Category of Improvement*

Group		No. of Patients
1	Improved on treatment. Relapsed on control	12
2	No change on control. Improved on treatment	16
3	Improved on treatment. Maintained on control	5
4	Improved on control. Maintained on treatment	4
5	Improved on treatment. Improved more on control ..	1
6	No change on control or on treatment	8
	Total ..	46

Note: Group 3 probably corresponds to group 1, but where the effect of treatment was prolonged into the control period.

When assessed according to diagnosis, there was no significant difference between the groups.

Comment on the Series

It was very noticeable that patients on treatment looked ill, with pinched, drawn faces, and pallor, though there was no subjective complaint.

Cases of pyrexia and tachycardia were much more frequent in the group receiving parenteral therapy. When an inflammatory area developed at the injection site, this was associated with pyrexia (four cases), but five more cases had temperatures of 100–103° F. (37.8–39.4° C.) (axillary), usually lasting four or five days and subsiding without other medication and without discontinuing the drug. Only two of the Group O cases had temperatures during the period of treatment.

TABLE IV.—*Liver-function Tests on Patient who Became Jaundiced*

Date	Van den Bergh Direct	Serum Bilirubin mg./100 ml.	Ser. Alk. Phosphat. Units	Thym. Turb. Units	Blood Urea mg./100 ml.	Protein (g.%)			
						Total	Alb.	Glob.	A/G Ratio
8/9	+	4·6	55·1	3·0	30	6·66	3·77	2·89	1·3:1
15/9		1·8							
24/9		1·5							
27/9	—	0·97	45·7	4·0	32	6·86	3·46	3·40	1·02:1
11/10	—	1·2	30·4	0·7	36	7·9	5·3	2·6	2·04:1

One case of jaundice has so far occurred. This first appeared 21 days after the beginning of treatment, and was preceded by two days' pyrexia to 102° F. (38.9° C.). The patient had received a total of 2,700 mg. of chlorpromazine at that time. It was noticed that her skin appeared yellow before the conjunctivae. A bradycardia down to 40 a minute developed, and persisted for three weeks. Urine was dark, but stools were not noticeably pale. Liver-function tests on this patient are shown in Table IV.

The following report is that of another patient who received chlorpromazine, developed jaundice, and then

recovered. Some weeks later she died of bronchopneumonia, an illness believed to have been quite unconnected with the jaundice.

A married woman aged 79 was admitted to a geriatric ward, where a diagnosis of senile dementia was made and she was given chlorpromazine both orally and parenterally. After 32 days, and after receiving a total dosage of 3,875 mg. in two courses separated by ten days, she developed jaundice. This occurred on the fourth day of the second course, when only 750 mg. of chlorpromazine had been given; treatment was discontinued. The jaundice subsided in two weeks. She was admitted to this hospital two months later, dying two weeks after admission. The cause of death, bronchopneumonia and pulmonary embolus, was confirmed at necropsy. Section of the liver showed nothing specific except moderate fatty changes and patchy lymphocytic infiltration in the portal areas.

Drowsiness, sometimes accompanied by a subjective giddiness, occurred in 11 cases. It usually passed off after the first two weeks, and in itself was not a serious complication. It was probably responsible, however, for the case of fractured neck of the femur. In elderly patients, in whom the risk of fracture is already present, the unsteadiness or drowsiness may well lead to a fall. This patient fell about one and a half hours after receiving her tablets. All patients were put to bed—though not all could be kept there—for an hour after receiving treatment, and this one fell soon after getting up.

Senile patients often become noisy, confused, and deluded after fractures, and chlorpromazine has been found very useful in such cases. It is noteworthy that, in the two cases in which fractures have occurred in elderly patients who were on chlorpromazine at the time, the common agitated, confused state did not develop. One of these has just been described, and the second case occurred while electroplexy was being given as well as chlorpromazine.

Other mild side-effects were dryness of the mouth, abdominal pain and diarrhoea, polyuria, and rashes. These responded to simple medication and did not warrant discontinuation of treatment.

Discussion

These results show that chlorpromazine has been effective in improving the general behaviour of a group of elderly psychotic women, though this improvement was not uniformly good. Most of them became more manageable, with few noisy outbursts or demonstrations of violence, and were able to feed and dress themselves. While several cases showed striking improvement, no patient in this group was considered fit for discharge, although two were going out with relatives for week-ends. Several patients have become employable, and have been able to take part in the social activities of the ward, the cinema, and coach rides.

It is necessary to compare these results with those which could be obtained using other forms of treatment at present available. Firstly, of course, these patients were chosen from those who had not responded adequately to other forms of sedation—all had been receiving large and frequent doses of paraldehyde or barbiturates, while several had had maintenance electroplexy. When they were included in the series and had this sedation stopped, many of them became very noisy and difficult; these patients were subsequently found to be having control tablets. Sedation by paraldehyde, barbiturates, or bromides suffers from the disadvantage that large doses are needed for long periods, and, even if the drugs are varied, problems of tolerance, habituation, drug rashes, and bromism arise. The patients are drowsy and confused, and unable to look after themselves, whereas after the first two weeks on chlorpromazine drowsiness usually passes off and the sedative effect seems to continue. After the drug has been discontinued the effect persists for a period varying from two to six weeks, and thus it may be possible to give periodic courses instead of continuous treatment. There seems to be no indication for routine parenteral therapy, even for a short introductory period, unless there is an urgent need to quiet a confused or agitated patient.

Adequate dosage is usually 150–200 mg. in divided doses daily, and the last dose should be given fairly late in the evening so as to ensure a good night's sleep.

I would like to stress the value of chlorpromazine in the treatment of restlessness following fractures in elderly patients. This is rapidly controlled, so that adequate operative and splinting technique may be carried out. It is in this type of case that the intramuscular route should be used, at least for the first few days. It is important to realize that in elderly patients, with the risk of fracture, use of the drug may be an additional hazard: it is little consolation to know that it is effective in the treatment of the condition it has helped to cause. Thus patients must be encouraged to rest for some considerable time after they have received their tablet—one to two hours if possible—and the dosage should be regulated so that the minimum is given to produce a therapeutic effect.

The question of the occurrence of jaundice is one of great importance. In this series there has been only one case (2%)—in fact, it is the only case that has occurred in this hospital, where at least 80 patients have received reasonably long courses of not less than 150 mg. of chlorpromazine daily. Until the action of the drug in the liver has been fully demonstrated, I feel that one should discontinue treatment while there is any sign of liver damage, and I would be reluctant to use it unless it was urgently indicated, in spite of the finding in the section of liver, which showed no evidence of permanent damage that could be attributed to the chlorpromazine. It is noted that in the other case described, where the patient died, there had been a pause in treatment, and jaundice recurred after treatment was renewed. The possibility of a sensitizing effect must be considered, especially as many psychotic patients, unless under careful observation, may not take all the tablets given and therefore dosage with the drug may only be intermittent.

It is difficult to understand why a demented patient should improve when taking chlorpromazine when she does not do so with other sedative drugs such as paraldehyde. The response is probably due to reduction in tension and response to hallucinations without alteration in the basic dementia. Thus, although the misinterpretations still occur, they are no longer charged with the same degree of tension and the patient can spare time to deal with her immediate surroundings. Sedative drugs merely damp down the cerebral response as a whole, while chlorpromazine acts selectively in a manner similar to the operation of leucotomy, for which reason it has been called the "chemical leucotomy." The possibility of its use as a therapeutic test for leucotomy, even if its effects do not persist, must be investigated.

The question of whether chlorpromazine can restore a chronic mental hospital patient to a condition of health sufficient to enable him or her to be nursed at home or in a home for the aged must also be considered. The patients described here were cases of extreme difficulty, and several of them have improved a great deal, though not enough for discharge. Experience with these, and with less difficult patients in the hospital, suggests that this drug may prove of much value for those patients who are still at home but tend to wander round the house at night and keep the rest of the family awake, or who are somewhat preoccupied with hypochondriacal symptoms. If this is so, it will go some way towards solving the problem of shortage of bed-space and of nursing staff in mental hospitals.

Summary

In a controlled experiment, where each patient acted as her own control, 46 elderly psychotic women were treated with chlorpromazine ("largactil"), and in 33 (71.7%) cases there was some degree of improvement. Two serious complications, jaundice and fractured femur, were considered, but were not thought to preclude the use of the drug as an aid in the nursing of the difficult patient.

I wish to thank Dr. R. E. Hemphill, medical superintendent, Bristol Mental Hospitals, for permission to use these cases; Dr. D. F. Early for his guidance and encouragement in preparing this paper; Dr. K. R. L. Hall for his help with the statistics; and Dr. W. Sandry for the report on the liver section. I also wish to thank the nursing staff, dispenser, and laboratory staff for their unfailing assistance, and Messrs. May & Baker for supplying the largactil and the corresponding control tablets and injections.

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L. CANICOLA INFECTION TREATED BY PENICILLIN

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Human infection with *Leptospira canicola* is infrequently recorded in this country although the organism is widely distributed in the canine population. Thus Stuart (1946) has shown that 25 to 40% of dogs in Glasgow are infected with the organism, and Broom and MacIntyre (1948) found similar figures in London. In dogs the organism produces a pyelonephritis, following which the animals may excrete the organisms in the urine for several months (Stuart, 1946).

The literature has been admirably reviewed by Broom (1951). He believes the infectivity to be low, since it is usual to find that only those in a household who have nursed an infected dog and who have cleaned up its dejecta are liable to contract the disease. Although the routes of infection are not known with certainty, the entry would appear to be through intact or broken skin, mucous membranes of the upper respiratory tract, or the conjunctivae. Bathing in contaminated water is a not uncommonly reported mode of infection.

The clinical features are those of an influenza-like illness of sudden onset, with signs of meningeal irritation appearing early in the illness in about two-thirds of cases (Alston, 1949).

We report two further cases arising in Glasgow. One of these was a laboratory infection, and it was possible to estimate the incubation period. Both were successfully treated with penicillin.

Case 1

Five days before admission to hospital a housewife aged 52 was suddenly taken ill with severe pains in the legs and paraesthesia from the knees to the ankles. On the second day of the illness she began to complain of severe throbbing frontal headache and pain in the neck. On the following day the pains and paraesthesia in her legs disappeared and were replaced by severe backache. On the fourth day of the illness persistent nausea, retching, and vomiting began, associated with an erythematous rash on her legs.

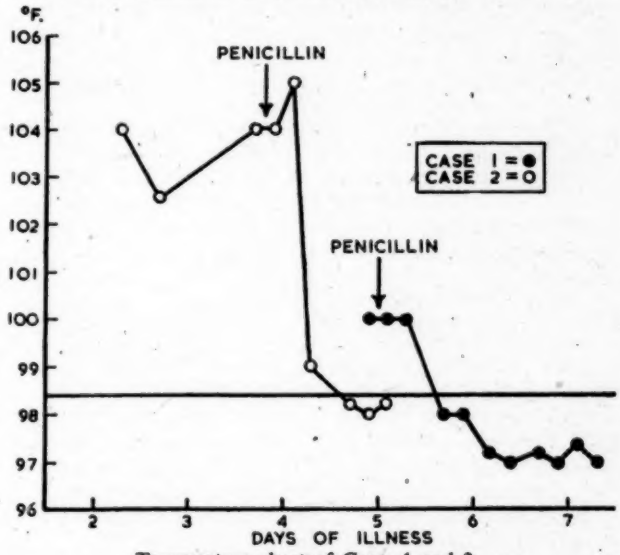
On admission to hospital she was found to be a flushed, rather drowsy woman with a pyrexia of 100° F. (37.8° C.). Discrete erythematous macules were present on the front of both legs, with a pin-point erythema over most of her back. The edge of the liver was palpable, as was the tip of the spleen. Slight neck rigidity was demonstrable. There was no jaundice. The total white blood count was 12,500 per c.mm. (85% polymorphs, 8% lymphocytes, 4% monocytes, 2% eosinophils). The E.S.R. (Westergren) was 40 mm. in the first hour. The urine showed no abnormality.

On lumbar puncture clear fluid was obtained at a pressure of 180 mm. of water. A pleocytosis of 584 cells per c.mm. (86% lymphocytes, 9% monocytes, 5% polymorphs) was present. The chemistry of the fluid showed: protein, 45 mg. per 100 ml.; sugar, 67 mg. per 100 ml.; and chloride, 725 mg. per 100 ml. No organisms were found microscopically or on broth culture.

During the two weeks preceding her illness the patient had been nursing a sick dog, and in view of this the veterinary surgeon who had been treating the dog was consulted. He stated that the dog had been suffering from a renal infection, and, whilst he had no bacteriological evidence of *L. canicola* infection, he thought this a likely diagnosis in view of the frequency of such infection among dogs in Glasgow.

In the light of this opinion, a provisional diagnosis of "canicola fever" was made, and, after blood specimens had been obtained for diagnostic purposes, treatment was instituted with crystalline penicillin, given intramuscularly in doses of 250,000 units six-hourly. This was begun one hour after admission—that is, on the fifth day of illness—and continued until the fourteenth day.

Within 24 hours there was relief of symptoms, and, after 48 hours, apparent clinical cure (see Chart).



Temperature chart of Cases 1 and 2.

Bacteriology.—The organism was not obtained on blood culture using ordinary media nor on guinea-pig inoculation, but serological tests confirmed the diagnosis in both the patient (Table I) and her dog, the latter's serum agglutinating *L. canicola* to a titre greater than 1/30,000. The same tests made on members of the patient's household, who had been in contact with the dog, were negative.

The patient was dismissed symptom-free two weeks after admission. A lumbar puncture carried out just before discharge showed a clear fluid under a pressure of 50 mm. of

TABLE I.—*Results of Serum Agglutination Tests in Two Cases of Leptospirosis Canicolaris*

	Case 1					Case 2			
Day of Disease:	5th	13th	23rd	50th	72nd	8th	19th	24th	44th
Reciprocals of titres with:									
L. canicola	0	1,000	10,000	1,000	1,000	Neg.	Neg.	1,000	1,000
L. icterohaemorrhagiae	0	0	10	0	0	,,	,,	100	30

water and containing 17 lymphocytes per c.mm. The chemistry of the fluid was normal. The patient showed no evidence of relapse after six months' observation.

Case 2

A lecturer in veterinary medicine aged 33 was suddenly taken ill with headache, shivering, and backache. On the second day of the illness the headache became much more severe and he vomited repeatedly. On this day he was seen at home by one of us, when the only findings were a pyrexia of 104° F. (40° C.), a tachycardia of 140 a minute, and some abdominal distension. There was no evidence of a meningeal reaction. He was treated expectantly with half-normal saline by mouth. On the third day of the illness he felt slightly better. The vomiting had stopped, though nausea, retching, and headache persisted. The temperature was now 102.6° F. (39.2° C.), but on the following morning the headache was again intense and retching severe. The temperature was now 104° F. (40° C.). The spleen was palpable three fingerbreadths below the left costal margin, and small pink macules 1 mm. in diameter were present on the skin of the abdomen. A specimen of blood was taken for broth culture. The white cell count was 7,400 per c.mm. (93% polymorphs, 6% lymphocytes, 1% monocytes). The urine contained albumin and a few erythrocytes. The E.S.R. (Westergren) was 40 mm. in the first hour.

At this point the patient was closely questioned about the possibility of having acquired any infection in the course of his work. He now remembered that seven days before the onset of the illness he had broken a tube containing a culture of *L. canicola* and in so doing had cut his finger. He had immediately washed the wound with a solution of penicillin.

It seemed probable that the patient was suffering from *L. canicola* infection, and after a further specimen of clotted blood had been removed for culture he was given one million units of crystalline penicillin intramuscularly.—Two and a half hours after the injection he had a very severe reaction. He felt very ill, and on taking his temperature found it to be 104° F. (40° C.). Immediately afterwards a severe rigor occurred which lasted about eight minutes. He felt extremely weak and was unable to feel his own pulse. After an hour he began to feel better, and, whereas previously he had been extremely restless, he was now content to lie still. Five and a half hours after the first injection of penicillin he was given a second dose of one million units. By this time he felt better, though he still looked very ill and had a temperature of 105° F. (40.6° C.). Two and a half hours later there was a marked improvement in his condition. His temperature was now 99° F. (37.2° C.), and his headache less severe (see Chart).

By the following morning (fifth day of illness) his improvement was remarkable. He had slept soundly, his appetite had returned, and the headache was only slight. The temperature was normal and the urine contained only a faint trace of albumin. The spleen was still palpable three fingerbreadths below the left costal margin.

The patient then made an uninterrupted recovery, the headache vanishing after three more days and the spleen soon becoming impalpable. He had received one million units of penicillin three times daily from the fourth to the seventh day of illness inclusive and the same dose twice daily from the eighth to the tenth day.

Bacteriology.—No growth was obtained from the broth culture. The specimen of blood clot was inoculated on to special media, and after four days' incubation *L. canicola* was isolated. The findings of serological tests carried out are shown in Table I.

Discussion

Pyrexia of Unknown Origin and Lymphocytic Meningitis

The ubiquity of *L. canicola* in this country is such as to make infection with this organism a possibility in every case of obscure fever. The clinical features, apart from the high proportion of cases of meningitis, are often indistinguishable from those of any septicaemia. The clue to the diagnosis lies in the history of contact with a sick dog.

That the leptospira may be the cause of a lymphocytic meningitis should also be borne in mind. Broom (1951) examined the sera of 642 cases of aseptic meningitis and found that 25 gave positive reactions for leptospirosis (17 *L. icterohaemorrhagiae*; 8 *L. canicola*). The report by the Virus Reference Laboratory, Colindale (1953), gives the following results of serological examination of cases of suspected virus infections of the central nervous system during 1949 and 1950.

Year	No. Tested	No. Positive for *Leptospirosis*	
1949 ..	130 ..	10 (7.7%) } 18	(6 *L. icterohaemorrhagiae*, 12 *L. canicola*)
1950 ..	196 ..	8 (4.0%) }	

This report suggests that increasing awareness of leptospirosis may be responsible for the lower figure of 1950, since sera were often sent direct to Dr. J. C. Broom and bypassed Colindale.

Minkenhof (1948), Broom (1951), and Joe and Sangster (1951) all emphasized the necessity for distinguishing between the meningitis of leptospirosis and that of non-paralytic poliomyelitis. Indeed, Alston (1949) reported that two-thirds of the cases of *L. canicola* infection in man showed signs of meningeal irritation. Broom and Joe and Sangster pointed out that a raised E.S.R., which is usual in leptospirosis, may be useful in excluding poliomyelitis where the sedimentation rate is usually normal. The raised E.S.R. in Case 1 illustrates this point.

Incubation Period

Kelser and Schoening (1948) showed that the incubation period of *L. canicola* infection in hamsters was 6–10 days. The incubation period has not, however, previously been accurately determined in man. The unique circumstances of the mode of infection in Case 2 would appear to place it at about seven days.

Treatment with Penicillin

The recorded cases of human infection with *L. canicola* between 1946 and 1951 which were treated with penicillin are enumerated in Table II. The results do not appear

TABLE II

Case No.	Author	Penicillin: Days of Illness*	Penicillin: Daily Dose (Units)	Result: Cure	Result: Relapse	Result: Failure
1	Rosenbaum (1946)	12–18	?	—	—	No significant effect
2	Baber and Stuart (1946)	6–9	60,000	—	68th day	—
3	Laurent *et al.* (1948)	6–10	600,000	—	16th day	—
4	" "	4–7	600,000	Alleviation of symptoms on 6th day	—	—
5	Weetch *et al.* (1949)	17–?	960,000	—	—	Patient died 24th day†
6	Mackay-Dick and Watts (1949)	8–15	2,300,000	—	17th day	—
7	" "	29–51 9–12	360,000 2,000,000	—	47th and 78th days	—
8	Campbell *et al.* (1950)	4–14	200,000	—	Recrudescence of fever during treatment	—
9	" "	8–16	200,000	Claim only modification of course of disease	—	—
10	Joe and Sangster (1951)	7–?	?	—	—	No spectacular benefit
11	" "	3–11	?	—	—	" — "
12	Fox and Fyfe (1951)	6–19	300,000	—	24th day	

* Days of illness are inclusive.
† Coincidental chronic nephritis.

encouraging. The difficulty in assessing the value of penicillin therapy is common to all conditions which tend to natural cure. It is especially difficult when different doses have been used and treatment has begun at different stages of the disease. In the case of *L. canicola* infections a further factor must be taken into account. McIntyre and Stuart (1949) have shown that in dogs there is an invasive or septicaemic stage followed by a later stage where there is renal involvement. Dogs in the first stage all recovered after penicillin treatment, but there was a 50% mortality if the kidneys were involved. The ineffectiveness of penicillin in the renal stage of the infection is further suggested by McIntyre and Montgomery (1952) and Brunner and Meyer (1949), who have shown that the organism can be recovered from the renal tubules 14 months to two years after treatment.

The very rapid response to penicillin in high dosage in our two cases strongly suggests a therapeutic effect. It is to be noted that both were treated early and were probably mainly in the septicaemic stage, although Case 2 showed some albuminuria. The severe reaction shown by Case 2 was of Herxheimer type, and is further evidence of a lethal effect on the organisms. It is perhaps significant that the only other recorded case of rapid improvement after treatment with penicillin (Case 4 in Table II) also received large doses early in the disease.

Stagg and Leibovitz (1951) believe that chlortetracycline ("aureomycin") is an effective therapeutic agent in *L. canicola* infection. The evidence for this is inconclusive, since in their case 18 hours of treatment with penicillin in high dosage had preceded chlortetracycline. In experimental *L. canicola* infection in hamsters, Heilman (1945) found that the protective effect of penicillin was greater than that of streptomycin.

Since no other satisfactory treatment is known, it seems desirable to treat recognized examples of this disease with large doses of penicillin as early as possible after infection.

Summary

Two cases of human infection with *Leptospira canicola* are described.

L. canicola infection should be considered in the differential diagnosis of unexplained pyrexia or lymphocytic meningitis.

Evidence is produced to show that the incubation period of the disease is about seven days and that the early administration of penicillin in high dosage is an effective form of therapy.

We are grateful to Dr. L. D. W. Scott, under whose care Case 1 was treated, for permission to publish, and for his helpful advice. We are also indebted to Dr. T. Anderson and Professor E. J. Wayne for their help in the preparation of this article and to Dr. J. C. J. Ives for his assistance in the bacteriological investigations.

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POLYAGGLUTINABILITY OF HUMAN RED BLOOD CELLS

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Amongst the abnormal agglutinations, polyagglutination is a rare phenomenon and few cases have been reported. It is a transitory agglutinability of red cells developed *in vivo* and characterized by the agglutination of cells by a proportion of normal sera independent of their group agglutinins. It is not connected with auto-agglutination.

In ABO blood grouping the so-called Landsteiner's law states that if an agglutinogen is present in the red cells of a blood the corresponding agglutinin must be absent from the plasma, and if the agglutinogen is absent the corresponding agglutinin must be present. The first part of this law is a logical outcome of the situation, for if both agglutinogen and agglutinin were present the cells would be agglutinated (Wright, 1952), but in cases of polyagglutination this law cannot and does not stand. This factor is known to appear in some diseased states, though it has been recorded in some healthy individuals as well, but in both cases it is found to be transitory. Whether there is any influence of this polyagglutinability on the diseased process is not yet known. It is very difficult to understand what initiates this agglutinability of these cells and why the process of agglutination is inhibited *in vivo* but initiated *in vitro*.

It has been described that *in vitro* the infection in a sample of blood may change the cells in such a way that they are agglutinated by all sera (Hübener–Thomsen–Friedenreich phenomenon). Friedenreich has shown that filtrates of certain bacteria contain an enzyme which acts on human red cells, changing a latent antigen to an active one, which is known as Friedenreich's T-antigen (Race and Sanger, 1954).

Case Report

A married Hindu woman aged 30 was admitted to Chittaranjan Seva Sadan Hospital on December 28, 1953. She had had four children, but no history of miscarriage or abnormal labour. Her first baby died a few years after birth; the other three are all living and in good health. Her menstrual history was normal. The last menstrual period was September 25, 1953. She had never had any transfusion. On admission to hospital she complained of pain in the lower abdomen for 22 days, bleeding per vaginam for 22 days, and fever for two days.

On examination the patient was very anaemic. There was no jaundice. Her temperature was 102.6° F. (39.2° C.) (the high fever continued until death), pulse 140, respirations 20, blood pressure 110/80 mm. Hg. A blood count showed Hb, 36%; red cells, 2,160,000; white cells, 13,400 (polymorphs 80%, lymphocytes 12%, monocytes 8%). The urine was acid in reaction and showed no abnormality.

Pelvic abscess was diagnosed and posterior colpotomy was performed. A substance like anchovy sauce was found. Microscopical examination of this showed inflammatory cells but no malignant cells. As transfusion was advised, the serum and the washed cells (suspended in normal saline) were tested, but in spite of repeated efforts we could not determine the group. The patient was Rh-positive with

C and D and negative with E antigen. The Kahn test was negative. The patient's cells were tested against α and β sera (Table I). The cells were agglutinated by both the sera, indicating Group AB, but when the serum of the patient was also matched against known cells A cells were agglutinated but there was no reaction with B cells (Table I), indicating Group B.

TABLE I

α Serum and patient's cells	..	..	+++	(agglutination)
β " " "	..	..	+++	"
A cells " " serum	..	..	+++	"
B " " " "	..	..	− − −	(no agglutination)

As the need for blood transfusion was urgent, and as no definite group could be determined, we tried to cross-match with 10 Group O bloods, 4 Group AB bloods, 10 Group B bloods, and 12 Group A bloods. The results are shown in Table II. All these tests were done repeatedly and in dilutions of 1 : 4, 1 : 8, 1 : 16, 1 : 32, but without any change of results either at room or at refrigerator (4 to 6° C.) temperature.

TABLE II

	Group O		Group AB		Group B		Group A	
	Serum	Cell	Serum	Cell	Serum	Cell	Serum	Cell
Patient's cells ..	+++	− − −	+++	+++	+++	− − −	+++	+++
" serum								

+, Agglutination. −, No agglutination.

The above grouping and cross-matchings were also done by the test-tube method at 37° C., but the results were the same as with the slide method. The serum and clotted blood of the patient were left in the refrigerator for more than one month at 4 to 6° C. and all the tests were repeated, but no change was detected. On all occasions her own serum did not agglutinate with her own red cells. The possibility of contamination can be excluded, as we performed all the tests immediately after the blood was withdrawn. The patient died on January 18, 1954.

Discussion

The first case of polyagglutinability was reported by Levine and Katzin (1938). They found that the red cells (Group O) of patients suffering from pneumococcus type I infection treated with sulphonamide and serum agglutinated with 15% normal sera independent of group. This peculiarity disappeared four months after recovery. Gaffney and Sachs (1943) reported two cases, of which one occurred in a patient with congenital syphilis and the other in a healthy adult. In both cases they found polyagglutination and concluded that both bloods were of Group O subjects.

Levine and Katzin's patient was also of Group O. In the first case of Gaffney and Sachs the titre of polyagglutinability went on increasing from 47 to 100%, in their second case it increased to 73%, and in both cases the cells and serum of patients agglutinated with both α and β serum and A and B cells respectively, but the cells failed to agglutinate at 37° C., thereby giving the correct grouping of the patient—that is, O. In neither case was there autoagglutination either at refrigerator or at room temperature. In all three cases this polyagglutinability was transitory and disappeared within four to six months.

In our case cells agglutinated with α and β serum and serum agglutinated with A cells but failed to agglutinate B cells and never agglutinated their own. We are thus inclined to describe the phenomenon here as polyagglutinability instead of panagglutinability.

Gaffney and Sachs found that the sera which agglutinated the cells of the patients at room temperature (20 to 25° C.) did not agglutinate at 37° C. This question does not arise in our country, because our room temperature is always around 37° C. In our case repetition of the tests in different dilutions and at our room temperature (34 to 37° C.) and at refrigerator temperature (4 to 6° C.) did not show any alteration in any way. This type of agglutination gives a false idea about the grouping of patients.

The cross-match report (Table II) gives a peculiar result, and no definite conclusion could be reached; in order to come to a conclusion we made a back calculation to suggest that the patient was possibly of Group B.

Observations of different authors at different times suggest that panagglutination is due to bacterial contamination. Schiff *et al.* (quoted by Gaffney and Sachs, 1943) produced panagglutinability of cells artificially by bacterial contamination, in which the red blood cells did not agglutinate with their own serum and thus the difference was only one of degree.

Though the existence of a relationship of cold agglutination with polyagglutination was suggested by different authors, our case did not show any such relationship, as we got the same result in different temperatures, including that of the room.

The actual pathogenesis of polyagglutination is far from certain, but we have already mentioned that the T-antigen is responsible for some such abnormal agglutination as is described by Friedenreich and supported by Henningsen, Holländer, Van Loghem, Van der Hart, and Heier (Race and Sanger, 1954). In our case the patient was dangerously ill and ultimately died of the disease; it seems possible that bacteria were in some way responsible.

It is evident from the above that previous authors got agglutination at room temperature but not at 37° C., but we found the same result at room temperature, at the refrigerator temperature, and at 37° C. incubation. As our patient was seriously ill, it seems that the degree of bacteriaemia or septicaemia might play some part in the phenomenon by transforming the latent T-antigen of cells into an active one. Further experimental work is necessary before any conclusion can be reached.

Summary

Polyagglutinability observed in a case of pelvic abscess with septicaemia is described and the relevant available literature reviewed.

The similarity between polyagglutinability and panagglutinability is observed and discussed.

The fact that such a case brings out the problem of correct grouping has been stressed.

T-antigen seems to have an aetiological bearing in such cases.

We wish to express our appreciation to Dr. A. E. Mourant, director, Lister Institute, London; Dr. R. Dutta-Choudhuri, pathologist, Chittaranjan Cancer Hospital; and Dr. Swadesh Basu, visiting surgeon, Chittaranjan Seva Sadan Hospital for Women. We thank Dr. Subodh Mitra, director, Chittaranjan Cancer Hospital, for his interest and help in this study.

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An unusual case is described in the latest (1954) annual report of the Medical and Dental Defence Union of Scotland Ltd. "A National Service candidate, aged 18, was referred by the examining board to an ear, nose, and throat specialist for an opinion. The latter, on examining the candidate when referred to him, undertook to wash out the candidate's antrum, a procedure to which the candidate's father objected, as having been done on a minor (or infant) without the parent's consent. While the claim was not pressed, the consultant was advised that he had been in error in his zeal, as he was entitled to do nothing more than furnish a report to the medical examiners who had referred the candidate."

VARICOCELES OF THE ROUND LIGAMENT IN PREGNANCY, SIMULATING INGUINAL HERNIAE

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It is worthy of note that swellings in the groin appearing for the first time in pregnancy do not seem to have attracted the attention of obstetricians and general surgeons. The similarity between femoral hernia and saphena varix is well recognized, but the likeness between a varicocele of the round ligament of the uterus appearing in the groin in pregnancy and an inguinal hernia appears to have been overlooked. A scrutiny of 16 standard textbooks in obstetrics, of 15 standard textbooks in general and operative surgery, North American and British, failed to reveal any comment. Textbooks on diseases of the vulva gave no information, and of the standard works on varicose veins only one made any reference to the subject, and then not specifically mentioning pregnancy: Verovitz (1941) states that "varices of the round ligament are often mistaken for an inguinal hernia." We believe we are describing a not uncommon condition which has been overlooked by clinicians, which is usually misdiagnosed, and which is omitted from the textbook literature.

The not infrequent occurrence of swellings in the groin, appearing for the first time in pregnancy and subsiding during the puerperium, had been noticed by us for some years. Although almost indistinguishable from an inguinal hernia on clinical examination, there seemed to be good reason to think that they were in reality varicoceles of the round ligament. Case 2, described below, stimulated our interest, so that medical officers in the antenatal clinics at Queen Charlotte's Maternity Hospital were asked to refer to us cases of "lumps in the groin." In a 12-weeks period 12 such patients were found and were followed through their pregnancy, labour, and post-natal period.

Case 1

This patient, aged 36, developed varicose veins of both legs during her first pregnancy in 1936. The veins subsided after delivery, returning during her next pregnancy, in 1951. During this second pregnancy lumps appeared in both groins, were diagnosed as herniae, and operation was advised. This advice was not taken.

She attended an antenatal clinic at Queen Charlotte's Maternity Hospital on July 27, 1953, in the 10th week of her third pregnancy, with a letter from her general practitioner referring her because of the history of inguinal herniae appearing in the previous pregnancy. On examination at that time the pregnancy was confirmed, notice being taken that varicose veins were present in both legs (including the upper thighs) and both labia majora. No mass could be produced in either groin, but a note was made that varicoceles of the groins were likely in view of the past history. The following notes were made during the remainder of the pregnancy, the labour, and the puerperium. August 27: Swelling in right groin present (Fig. 1) diagnosed as a varicocele. September 24: Swelling in both groins, aching at the end of the day. A dragging sensation and aching in the groins continued until delivery. March 5, 1954: Spontaneous vertex delivery; total duration of labour, 2 hours 25 minutes. March 12: Varicose veins improved, slight lump present in each groin. April 8: Very little swelling present in groins. May 3: No swelling present in either groin (Fig. 2).

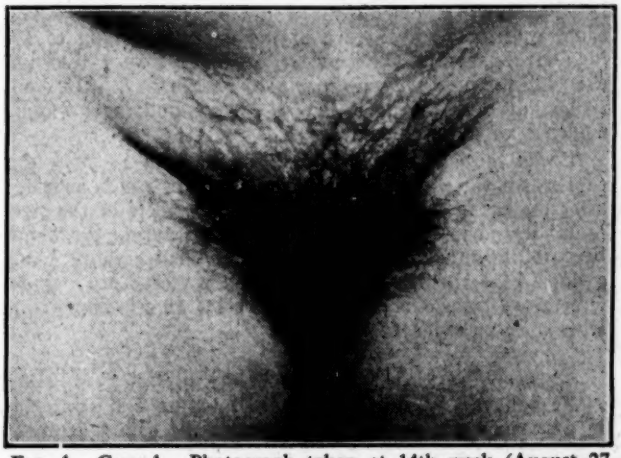

FIG. 1.—Case 1. Photograph taken at 14th week (August 27, 1953), showing a swelling in the right groin.

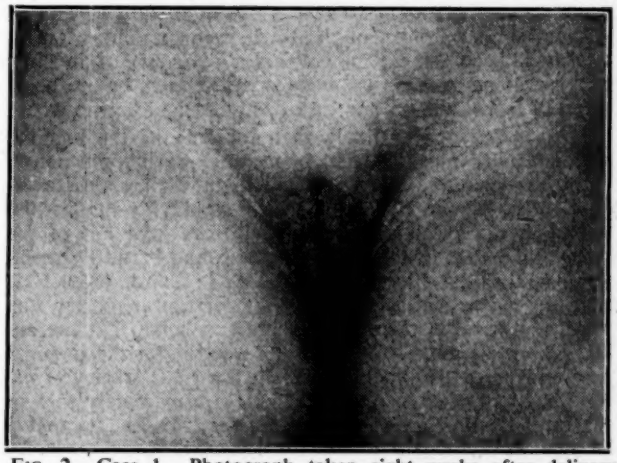

FIG. 2.—Case 1. Photograph taken eight weeks after delivery (May 3, 1954).

Case 2

A patient, aged 27, pregnant for the first time, was booked for delivery at Queen Charlotte's Maternity Hospital, the expected date of delivery being February 16, 1953. Until October 6, 1952, no abnormality was detected, but on that attendance at the clinic the patient complained of a lump in the left groin; she was referred to an obstetric consultant, who diagnosed a left inguinal hernia, suggesting no active treatment. On January 1 varicose veins of the vulva were first noted.

At 9.40 a.m. on February 16 there was a spontaneous vertex delivery of a living female infant after a labour lasting 9 hours 50 minutes.

During the forenoon of the 17th the patient complained of pain in the right lower abdomen. On examination a tender mass was present in the right groin, measuring 1½ in. by 1 in. (3.8 by 2.5 cm.), irreducible, and diagnosed as a right inguinal hernia. At 5.30 p.m. the mass was unchanged, with normal bowel sounds. The opinion of a general surgeon was obtained, and at 9.30 p.m. he operated, the

provisional diagnosis being an irreducible right inguinal hernia. Under general anaesthesia a right oblique inguinal incision was made, dividing the right external oblique aponeurosis. This exposed the mass, which was found to be a collection of thrombosed vessels in the substance of the round ligament. This was divided, excised, and ligated at the internal abdominal ring. A small hernial sac was found to be empty; it was transfixed and excised. The inguinal canal was closed by suture of the conjoint tendon to the inguinal ligament. The post-operative recovery was uneventful, the patient leaving hospital on March 2. On April 14 healing of the right groin was perfect, and there was no evidence of a left inguinal mass.

It was thought that the "left inguinal hernia" in this case was a varicocele of the round ligament which subsided after the pregnancy, whilst a smaller varicocele of the right round ligament which was not discovered during pregnancy became thrombosed immediately after delivery, probably owing to the alteration in the size of the uterus producing a circulatory disturbance; both varicoceles were in association with varicose veins of the vulva.

Discussion

We believe that nearly all groin tumours first appearing in pregnancy are due to varicosities of the round ligament, which at first sight simulate an inguinal hernia. While in 2 out of the 12 cases under review there was little evidence of varicose veins, apart from the varicocele of the groin, in the remaining 10 varicosities of the vulva, with or without similar lesions of the thigh, were present, often to a gross degree. In seven patients a diagnosis of inguinal hernia was made when the mass was first seen, before being referred to us, and in one case operation had been advised.

It does not appear likely that a hernia of the inguinal region should make its first appearance during pregnancy, for, although there is an increase in intra-abdominal pressure, most of the structures which would fill the hernial sac (with the exception of free fluid) are kept out of the way by the bulk of the pregnant uterus and broad ligament. Some authorities (Berkeley *et al.*, 1938; Baird, 1950) state that pre-existing herniae frequently disappear during the later months of pregnancy, "the reason being that the enlarging uterus pushes the intestines away from the inguinal ring and presently blocks access to them" (Berkeley *et al.*, 1938). Strangulated inguinal herniae are extremely rare in the later months, and, in fact, Gaudier (1894) states that a strangulated inguinal hernia and pregnancy are incompatible. Although it is generally agreed that known pre-existing herniae tend to be temporarily cured during pregnancy, this series of 12 cases of swellings in the inguinal region first appearing in pregnancy was collected in the short space of 12 weeks. It is known that early in pregnancy, in the first trimester, there is a great increase in the vascularity of the pelvis, and varicose veins of the lower extremity may appear or worsen before the size of the uterus is likely to affect the venous return. The veins of the round ligament form an anastomosis with those of the vulva, and will join in any generalized varicosity—thus a varicocele of the round ligament is formed.

Clinical Features.—The clinical features of varicoceles of the round ligament are similar to those of an inguinal hernia. The patient complains of a lump and an aching feeling in the groin. The situation is identical, since both veins and hernial sac accompany the round ligament in the inguinal canal. Both swellings disappear on lying down and reappear on standing, though a varicocele may return more gradually than a hernia and is a little less circumscribed. A varicocele is of course dull on percussion and more closely resembles a hernia containing omentum than one containing bowel. The signs and symptoms of both conditions are therefore very similar, and it is only possible to make a diagnosis by the fact that in the case of the varicocele the swelling appears for the first time during pregnancy. The absence of varicose veins elsewhere does not exclude the diagnosis of a varicocele of the round ligament. Thrombosis of the varicose veins is a complication which still further increases the resemblance between an inguinal hernia and varicocele of the round ligament, and is described in Case 2. This complication produces a firm, tender, irreducible swelling simulating a strangulated inguinal hernia, and a differential diagnosis becomes an urgent necessity, in view of the entirely different treatments required.

Treatment.—No active therapy has been found necessary in the patients we have seen. Suggestions to operate during pregnancy indicate that the probable aetiology of the lesion has not been appreciated. It is not necessary to commit a patient to bed rest because of the condition, although it is known that this occurred in a patient elsewhere, not in our series, in the belief that an inguinal hernia was present. A truss may, by giving support, add to the comfort of the patient. Reassurance, with a simple explanation of the temporary nature of the lump during pregnancy, and the recommendation of the usual supportive measures for the relief of vulval and leg varicose veins, is all that has been found necessary.

We wish to express our thanks to members of the clinical staff of Queen Charlotte's Maternity Hospital for helping to collect the cases, and to Mr. Bailey, of Queen Charlotte's and Chelsea Hospital photographic department, for the photographs.

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THE SYMMETRICAL FORM OF STATUS BONNEVIE-ULLRICH (TURNER'S SYNDROME)

BY

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In 1930 Ullrich reported a case of multiple congenital anomalies in an 8-year-old girl that was typical of a syndrome since known on the Continent as the symmetrical form of status Bonnevie–Ullrich. This child was of short stature, had a webbed neck (pterygium colli), an increased carrying angle of the arms (cubitus valgus), hypoplastic nipples, a highly arched palate, drooping angles of the mouth, hyperflexibility of the shoulder-joints, and irregular short nails of the hands and feet. The upper eyelids were prominent and heavy, giving the impression of bilateral ptosis. The ears were closely attached to the side of the head. At birth there had been a marked pitting oedema of the nuchal region and the extremities. The oedema, "congenital lymphangiectatic oedema," disappeared during the second year of life.

Ullrich (1949) observed that this syndrome is identical with Turner's syndrome and the syndrome of ovarian agenesis, which have since been described and discussed in the English language literature by authors evidently unaware of his original report. It is apparent, however, that, whereas Ullrich (1930) described the congenital anomalies in great detail, it was the endocrinological aspects which aroused most interest in the American

and British literature. It is our purpose to present a typical case of this syndrome occurring in an African infant.

Case Report

A 3-weeks-old Bantu female was first seen on April 8, 1953. The mother complained that the infant had been "swollen" since birth.

Physical Examination.—Head: The circumference of the head was 14 in. (35 cm.). There was marked pitting oedema of the scalp, especially over the occipital region. Some oedema was present round the eyes, and the epicanthic folds were prominent. The bridge of the nose was flattened and somewhat broad. The corners of the mouth were drooping and the palate was highly arched. The upper parts of the ears were bound to the margin of the scalp. The superficial scalp veins were unusually conspicuous and large. The cranial nerves appeared normal. *Neck:* There were broad loose folds of skin over the postero-lateral aspects of the neck (pterygium colli). The occipital hair-line was low. *Chest:* The skin over the whole of the back was loose (cutis laxa). The chest was somewhat broad in shape. The nipples were hypoplastic, being pin-point in size. The heart and lungs were clinically and radiologically normal. *Abdomen:* The tone of the abdominal musculature was normal. A small umbilical hernia was present. *Extremities:* There

Photograph showing pitting oedema of the extremities.

was marked pitting oedema of the extremities (see Fig.). The nails of the fourth and fifth toes of the left foot and the fifth toe of the right foot were absent. The remainder of the nails of the hands and feet were spoon-shaped. There was a laxity of all the joints of the limbs, and the elbow-joints could be passively placed into a marked degree of cubitus valgus. *Genitalia:* The external genitalia appeared normal.

Investigations.—The urine was normal. Haemoglobin, 13 g. per 100 ml.; blood urea, 10 mg. per 100 ml.; serum proteins, 6.8 g. per 100 ml. (albumin 3 g., globulin 3.8 g.); thymol turbidity test, 1 unit; thymol flocculation, Takata–Ara, and colloidal red tests were negative; serum sodium, 350 mg. per 100 ml. *X*-ray plates of the spine, skull, and extremities showed no skeletal abnormalities. The mother's Wassermann reaction was negative.

Examination of Family.—The parents and the two other siblings were examined clinically and radiologically. The upper parts of the ears of the father and both children were closely attached to the scalp margin, but no other abnormality was observed.

Progress.—When the child had been in hospital for one month she developed gastro-enteritis, which lasted for three days. During this period the oedema disappeared completely and recurred only when the diarrhoea and vomiting had stopped. She was discharged six weeks after this. When seen again, at the age of 6 months, the child was in good health and mental development appeared to be normal. The circumorbital and nuchal oedema had disappeared, but pitting oedema of the extremities was still prominent.

Discussion

Turner (1938), unaware of Ullrich's report, described a triad characterized by webbing of the neck, cubitus valgus, and infantilism which he had observed in seven adult females. Numerous similar cases have since been reported by others (Sharpey-Schafer, 1941; Albright *et al.*, 1942; Varney *et al.*, 1942; Wilkins and Fleischmann, 1944; Lisser *et al.*, 1947; Del Castillo *et al.*, 1947; Dorff *et al.*, 1947; Jackson, 1950; Jackson and Sougin-Mibashan, 1953). Congenital anomalies observed by these authors, in addition to the webbed neck, cubitus valgus, and short stature emphasized by Turner, included the low hair-line at the nape of the neck, dystrophies of the ears, "shield" chest, arched palate, scoliosis of the spine, and coarctation of the aorta. Cases in a few females under the age of puberty were also recognized (Goldberg *et al.*, 1947; Silver, 1951; Cutler and Silver, 1953; Jackson and Sougin-Mibashan, 1953; Vulliamy, 1953).

Some authors have apparently avoided the term "Turner's syndrome"—firstly, because Turner (1938) considered that the sexual infantilism was of pituitary rather than gonadal origin, and, secondly, because congenital webbed neck or cubitus valgus was not invariably present. However, the term "syndrome of ovarian agenesis" is even more unsatisfactory, as the condition has been observed, though less commonly, in males (Flavell, 1943; Dorff *et al.*, 1948; McCullagh, 1948; Greenblatt and Nieburgs, 1948; Reforzo-Membrives *et al.*, 1949; Sohval, 1951; Cunningham and Harley, 1951; James, 1952; Sougin-Mibashan and Jackson, 1953; Mackenzie, 1953). It is possible that the term "Bonnevie–Ullrich–Turner syndrome," as suggested by James (1952), would do most to clarify the present somewhat disjointed situation and combine the contributions to the subject from both the Continental and the English language literature.

Our patient has shown virtually all the salient features of the syndrome as listed by Ullrich (1949). This author emphasized the frequency with which the "congenital lymphangiectatic oedema" occurs, and considered the formation of this subcutaneous fluid during prenatal life to be the main aetiological factor in the various congenital anomalies seen. In over a hundred patients reported in the English language literature, however, we have found reference to oedema in only two case reports. Silver (1951) stated that the feet of his patient, aged 2 years and 8 months, were described as having been "swollen" at birth; and Vulliamy (1953), in his report of an 8-year-old girl, described "unexplained oedema of hands and feet at birth, persisting in the feet for the first three years." Pitting oedema was a very prominent feature in our patient, and was, in fact, the reason that the mother sought medical advice. It is difficult to understand how, if it were present, such a conspicuous abnormality could have been so frequently overlooked. Ullrich (1949), however, stated that the swelling disappears during the first two years of life. As our patient is the first under the age of 2 years whose case is described in the English literature, this may well explain why oedema has so seldom been mentioned.

No definite hereditary factor has yet been discovered. Unfortunately we were able to trace only our patient's immediate relatives, but were impressed by the complete attachment of the upper parts of the ears to the scalp margin in the father and the two other siblings. This particular anomaly was seen by Sharpey-Schafer (1941) in his patient; it is apparent to a moderate degree in the photograph of the male patient of Sougin-Mibashan and Jackson (1953), and is well marked in the male African reported by Mackenzie (1953). Whether this ear anomaly represents a very mild form of the syndrome in the relatives of our patient it is at present impossible to determine, but it was considered distinct enough to merit being put on record.

ADDENDUM.—Since this paper was written a case of this syndrome associated with hypertrophic pyloric stenosis has been recognized in a 2-months-old infant (Keay and Lewis, 1954). These authors, however, described the oedema of the extremities in their patient as non-pitting in character.

We are indebted to Dr. J. D. Allen, superintendent of the Baragwanath Hospital, for permission to publish this report. We wish to thank Dr. E. Kahn, under whom the patient was admitted, for his encouragement and advice.

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Medical Memoranda

"Primary Myxoedema" in a Man of 30

Myxoedema was first described by Gull (1874) when he wrote "On a Cretenoid State Supervening in Adult Life in Women." It was Ord in 1878 who first used the term "myxoedema" to describe these cases of hypothyroidism. It is well known that myxoedema generally occurs in middle-aged and elderly women. Myxoedema in young males is uncommon, and so far as can be ascertained is either due to "pituitary myxoedema" as described by Means *et al.* (1940) or present as a true myxoedema following total thyroidectomy. It is therefore most unusual to find a case of "primary myxoedema" in a man of 30.

FIG. 1 FIG. 2

FIG. 1.—Photograph taken on October 23, 1953. FIG. 2.—Photograph taken on November 28, 1953.

CASE REPORT

A gardener aged 30 was first seen in consultation in October, 1953. He complained of a rash on the hands and forearms which was due to a plant-contact eczema. His general appearance was most striking, as shown in Fig. 1. On further questioning he admitted to the following symptoms: (1) the gradual onset during the past two years of increasing weariness, which was now extreme towards the end of the day; (2) increase in weight; (3) a preference for hot weather and a feeling of the cold "right through him"; (4) a deepening of his voice and a slowing and hesitant speech; (5) a drying of the skin—"he had not sweated for months"; and (6) his hair was becoming coarse and lifeless.

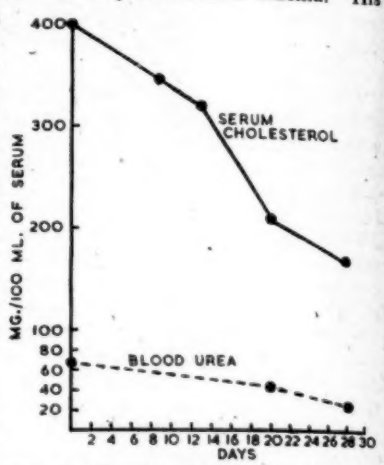

FIG. 3.—Showing improvement in blood chemistry.

On examination there were no physical abnormalities apart from a bradycardia of 50. The serum cholesterol was 400 mg. per 100 ml. and the blood urea 67 mg. per 100 ml. of serum. Examination of the urine showed: sp. gr. 1009, sugar, nil; albumin, slight trace; no casts or red blood cells. *X*-ray examination of the pituitary fossa was normal.

Treatment with L-thyroxine sodium 0.1 mg. daily for a week, then 0.1 mg. twice a day, was started on October 23. Improvement was most dramatic, both in his appearance as shown in Fig. 2, taken five weeks after Fig. 1, and in the blood chemistry as shown in Fig. 3, the serum cholesterol and the blood urea returning to normal within twenty-eight days.

He felt perfectly fit and all his symptoms had disappeared. His voice was now normal, he could sweat, his hair was improving in texture, he had lost weight, and he was no longer weary.

COMMENT

This record is of particular interest as it describes a case of "primary myxoedema" in a young man which responded dramatically to a relatively small dose of thyroxine and showed a fall, not only of the serum cholesterol as would be expected, but also of the blood urea. The fall in the blood urea was presumably due to the increased metabolism. Or could it have been due to a clearing of "cholesterol-clogged" arterioles in the kidneys?

I am grateful to Dr. C. A. K. Bird, of Macclesfield Hospital, for his advice and help with the blood chemistry in this case.

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Ventricular Tachycardia following Exercise in a Case of Angina Pectoris

It is felt that the following case is interesting enough to be placed on record.

CASE REPORT

A man aged 46 attended the out-patient department giving a history typical of angina pectoris of four months' duration. The attacks had never occurred before this, had on no occasion lasted longer than 10 minutes, and had never been severe enough to cause absence from work. Apart from "pleurisy" 10 years previously, no history of any past

illness was obtained. He worked as a light machinist at a lathe in a nearby factory. He was married and had a family of four sons. No familial history of any ailments was obtained.

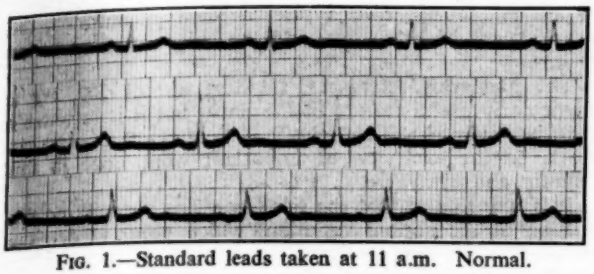

FIG. 1.—Standard leads taken at 11 a.m. Normal.

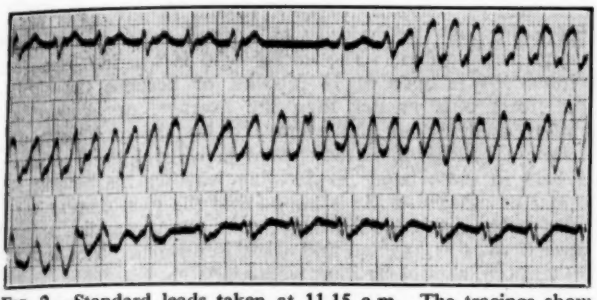

FIG. 2.—Standard leads taken at 11.15 a.m. The tracings show ventricular complexes which vary in size and which are deformed, the appearances being those of ventricular tachycardia or ? flutter. Rate 330 a minute.

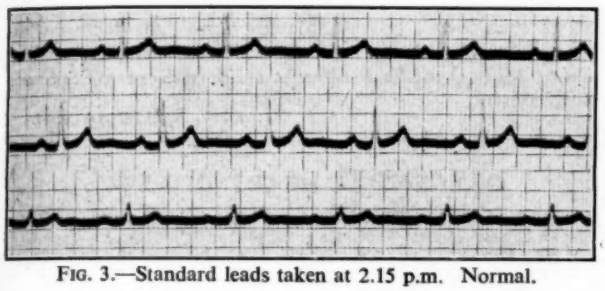

FIG. 3.—Standard leads taken at 2.15 p.m. Normal.

Little of significance was found in the various systems, but examination of the cardiovascular system revealed: pulse, 70, regular, good volume and tone, arterial wall normal; blood pressure 150/100; apex beat displaced slightly downwards and outwards; a soft systolic murmur audible over the apex. Fundi: early silver wiring and tortuosity of the vessels.

Investigations.—Hb, 110%; white cells, 9,000; E.S.R., 19 mm./hour. W.R. and Kahn test negative. Urine normal. Chest *x*-ray examination showed no active disease in the lung fields; slight tenting of the right diaphragm was due to a minimal adhesion; the heart shadow was normal. Electrocardiograms were taken (1) before exercise (Fig. 1); (2) after exercise which caused a typical attack of retrosternal pain with sweating and coldness; the symptoms were relieved by inhalations of amyl nitrite (Fig. 2); and (3) 3¼ hours after exercise (Fig. 3).

Trinitrin tablets for individual attacks, and quinidine sulphate, 6 gr. (0.4 g.) three times daily, have been given since. Up to the time of writing the patient managed fairly well, although he still had occasional tightness of the chest.

COMMENT

Schwartz (1942) describes three phases in the production of ventricular fibrillation—ventricular tachycardia proceeding to multifocal ectopic beats and eventual establishment of ventricular fibrillation. The ectopic beat prior to the run of tachycardia (initial premature beat) bears a constant relationship to the preceding ventricular complex, and all such beats appear to be identical in form and direction.

Runs of ventricular tachycardia are thought to originate from an irritable ventricular focus, and are the precursor of fibrillation.

Wetherbee *et al.* (1952) published tracings showing ventricular tachycardia following quinidine therapy in six cases of auricular fibrillation. Schwartz *et al.* (1953) showed tracings of transient ventricular fibrillation following quinidine therapy in cases of atrioventricular dissociation. A case of complete heart block described by Gresham (1952) gave rise to a series of electrocardiograms showing, at first, runs of ventricular tachycardia but, terminally, evidence of ventricular flutter and fibrillation.

The case described would appear to be in the first phase described by Schwartz in the production of ventricular fibrillation, and it is interesting to postulate an irritable ventricular focus arising from recurring relative ischaemia of a patch of ventricular musculature.

I wish to express my sincere thanks to Dr. Robert Mowbray for his constant help and permission to publish this case. I would also like to thank both the secretarial staff and members of the E.E.G. department, Dryburn Hospital, for their valuable assistance.

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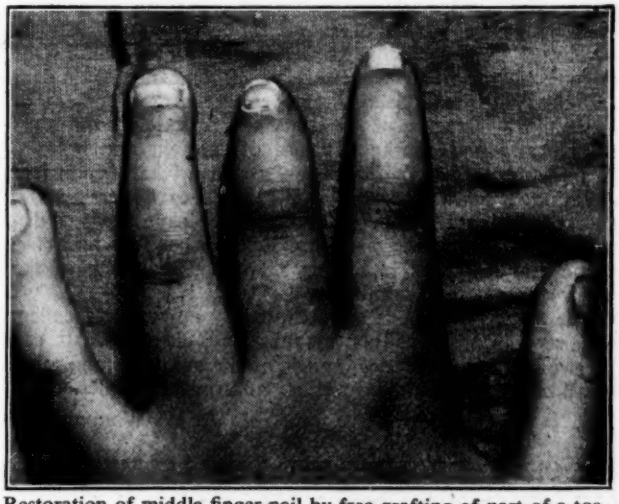
Grafting of Finger-nails

The restoration by grafting of lost or congenitally absent finger-nails is a subject upon which very little has been written. After carrying out a series of experiments it may be of interest to record that in suitable cases either the whole or part of the toe-nail can be transferred to the finger or thumb.

Apart from the disfigurement associated with absence of a nail, there is often a considerable reduction in function in the finger-tip. The normal nail acts as a support to the highly sensitive pulp, and without this counter-pressure the finer qualities of tactile appreciation are blurred. In the index finger or thumb this may be a very real disability in fine work.

The example shown here is the hand of a girl aged 8 in whom the middle finger showed congenital absence of a nail associated with brachydactyly (fusion of the distal and middle phalanges). Part of the great toe-nail with its



Restoration of middle finger-nail by free grafting of part of a toe-nail. One year after operation.

germinal matrix was implanted on the finger, and one year after the operation is seen growing normally. The donor toe-nail has also regenerated and causes her no discomfort.

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Reviews

TROPICAL ARCHITECTURE

Conference on Tropical Architecture, 1953. A report of the Proceedings of the Conference held at University College, London, March, 1953. (Pp. 144; illustrated. 32s.) London: George Allen and Unwin, Ltd. 1954.

The problems presented by tropical architecture are as numerous and as varied as is the scene in tropical towns, packed as they are with innumerable forms of life and activity. The demand for a place in the jostling life of these towns is increasing, for, as Mr. C. Y. Carstairs states in an admirable introduction to this publication, one of the results of public order and better preventive and curative medicine latterly introduced into the Tropics has been a steep rise in population, and people unable to find a living on the land are crowding to the towns. "The expanding populations of the world cannot be fed unless more food is produced more efficiently by fewer farmers and peasants." Thus thousands are "extruded from an agricultural economy which no longer needs them." A tremendous social problem is being treated and must be tackled by promoting industrial development and planned housing schemes if the squalor of disorderly, insanitary, shanty-town slums is to be avoided. At this conference these and related problems were discussed, and the many subjects dealt with included the tropical aspects of planning, indoor climate and thermal comfort, style in architecture, traditional and modern building materials and construction, new building techniques, building with timber, and architectural education and training. On all these there are excellent papers which will be of interest, not only to architects and town planners, but to sociologists, educationists, and medical men. Professor Crowden reviews physiological principles underlying thermal comfort in the Tropics—a subject of importance to all who dwell in such regions, and one of which he has made a special study. Application of these principles to architecture has been attended by very good results.

Since the war several new towns and townships have been built, and already considerable experience in modern methods of construction and planning has been obtained and is here discussed. Problems very different from those encountered in temperate regions have had to be faced; thus the green open spaces so pleasant in temperate regions, and in tropical countries in which there is a high rainfall, in an arid climate become barren and dusty and are then used as public latrine areas or rubbish dumps. Underdeveloped regions often being synonymous with poor regions, financial stringency is usual, and much thought and ingenuity have been directed towards development of economical methods of ventilation, protection from dust storms, and making the best use of sunlight and breezes. A possible criticism of the conference is that insufficient attention appears to have been devoted to discussing and to encouraging research in domestic drainage, sewage disposal, and those aspects of building designed to limit fly-borne and intestinal infections. These remain one of the major sources of disability in the Tropics.

The book throughout is illustrated by numerous excellent and very informative photographs and diagrams. It can be strongly recommended, and is of the greatest importance to all concerned with the welfare of tropical peoples.

A. W. WOODRUFF.

CHILD GROWTH AND DEVELOPMENT

Growth and Development of Children. By Ernest H. Watson, M.D., and George H. Lowrey, M.D. Second edition. (Pp. 296; illustrated. 53s.) Chicago and London: The Yearbook Publishers Inc. 1954.

This is a second edition of a book the first edition of which has fully established its worth and has found its place in the reference libraries of teaching schools and on the shelves of paediatricians. In this edition the authors have introduced changes in the chapter on physical growth and a new and valuable chapter on the growth and development of the face, jaws, and teeth, and on tooth eruption and malocclusion. The book gives a useful summary of knowledge on physical growth, including the development of organs and bones, with a brief account of nutrition, the development of behaviour, and the role of the endocrine glands.

The numerous references, totalling almost 300, are a particularly useful feature of the book, but it is regrettable that they refer almost entirely (in 96% of cases) to American work, to the exclusion of important work done in this country and elsewhere.

It is unfortunate that the book contains virtually no discussion of the normal variations which occur in development. For instance, on page 132 it is stated without reservation that in the normal child the anterior fontanelle is obliterated on palpation between 10 and 16 months of age. This is true of the majority of normal children, but not by any means of all. The doctor who is worried because a fontanelle is open at 18 months, or because the skull circumference is greater than the average, or because a child is smaller than the average in weight or height, or because a child is later than usual in walking, will receive no help in these pages in deciding whether his patient is normal or otherwise. It is hoped that the next edition will remedy this defect and attempt to draw some distinction between what is average and what is normal. The index, furthermore, should be improved.

This is hardly a book for the expert who has a special interest in any of the various aspects of development which it discusses, for the subject is such a wide one that it inevitably deals superficially with each item; but it does give an excellent bird's-eye view of development as a whole, and as such it will be valuable for almost all doctors who are concerned with the care of children, whether paediatrician, school medical officer, child welfare officer, or family doctor.

R. S. ILLINGWORTH.

CONGENITAL HEART DISEASE

Congenital Heart Disease: An Illustrated Diagnostic Approach. By Henry S. Kaplan, M.D., and Saul J. Robinson, M.D. (Pp. 126+xii; illustrated. £5.) New York, Toronto, London: McGraw-Hill Book Company, Ltd. 1954.

This book is yet another addition to the fairly numerous "atlases" of congenital heart disease that have appeared from several countries during the last few years. Its authors are respectively Professor of Radiology and Assistant Professor of Paediatrics at Stanford University School of Medicine, San Francisco.

It consists of two sections: the first is a presentation of the clinical features of various diagnostic procedures used in congenital heart disease, and the second a radiological atlas. The first section is in general excellent, the material being presented clearly and concisely; the atlas portion is well arranged, with drawings superimposed upon the cardiac shadow to demonstrate the position of the chambers and great vessels. The idea is good, but the angiocardiograms on which the atlas is based are of very poor quality and quite unconvincing; most show a merely formless opacity, much below the standards expected to-day. The aortograms of aortic coarctation are, for instance, just dreadful, whereas it is possible to show the lesion clearly and unequivocally. There is similarly no real demonstration of the lesions in Fallot's tetralogy or in pulmonary valve stenosis.

Like its fellow-atlases, this book is of approximately quarto size—a habit that seems to have grown upon us. It is an awkward size for handling, reading, and storing on the shelf. There seems no reason why a smaller and more convenient size could not be used.

The publishers state that it is intended primarily for the general practitioner and medical student. Its whole format is very suitable for direct, concise student teaching, and in this it succeeds admirably. The expert will find but little

in it for him. For students the price seems rather high, although the abundant illustrations make a high price inevitable. They will have to rely upon borrowing it from a library.

RUSSELL BROCK.

A SELFLESS SURGEON

The Scalpel, the Sword: The Story of Dr. Norman Bethune. By Sydney Gordon and Ted Allan. (Pp. 271+xv; illustrated. 16s.) London: Robert Hale Ltd. 1954.

Dr. Norman Bethune was born of pious Presbyterian parents at Gravenhurst in Ontario in 1890. By dint of working during vacations as a waiter or lumberjack he was able to study medicine at a university. Before he was qualified he served in the first world war as a stretcher-bearer in a Canadian field ambulance. He was wounded at Ypres, and on being invalided home obtained his medical degree and then served as surgeon-lieutenant in the British Navy. When the war was over he came to London and took the F.R.C.S. After marrying a young Scots lady of good family he returned to the New World and settled in practice in Detroit, where he gained a surgical reputation at the local hospital. He was then laid low by pulmonary tuberculosis, and while in a sanatorium read the writings of Dr. E. Alexander. He thereupon "stormed into the administrative building" and insisted that an artificial pneumothorax should be performed upon himself. This was done and he speedily got well. After his recovery he worked with Archibald, the famous thoracic surgical pioneer, and himself soon achieved success in that branch of surgery. He and his wife were divorced, but remained friendly.

Bethune was impetuous and irascible. He was impatient, and sometimes angry, with those who did not share his views. He had within him the missionary zeal, but not the doctrinal beliefs, of his godly parents. He became disgusted with ordinary practice and thought a State service was needed. He became a Communist, and, consenting to act as surgeon to the Spanish Republican Forces, did good work in arranging a transfusion service. Then he toured America and lectured in order to obtain funds for the Spanish cause. Finally, in 1938, he went to China to organize the surgical arrangements for the guerrilla Communist Forces. After almost two years of incredibly hard and self-sacrificing work he died of septicaemia in 1939 at the early age of 49.

The first part of this book deals with Bethune's early life and work in Spain; it is rather diffuse, and, while it may be attractive to a lay reader, is likely to be irritating to the medically qualified because of its melodramatic style and the unusual values it puts upon medical attainments and things in general. The second part, which deals with Bethune's experiences in China, is more restrained, and gives many extracts from his own writings penned in China. We see him here as a competent, selfless, hard-working surgeon who was absolutely devoted to his patients. On several occasions he continued operating, with scanty assistance and poor equipment, for two days continuously. His improvisations, his method of operating near the front line, his remarkable use of blood transfusion under the most difficult circumstances, stamp him as a pioneer. Dr. Richard Brown said of him: "Norman Bethune boasted that he was a Communist. I say he was a saint of God." To the reviewer the second part of the book was a delight and compensated for the rather turgid style of the first part.

ZACHARY COPE.

NATIONAL INSURANCE IN AUSTRIA

Praxis der Begutachtung. By Simon Mayr. Foreword by Lorenz Böhler. (Pp. 73+xi; illustrated. D.M.20.) Vienna, Bonn: For Medizinische Wissenschaften by Wilhelm Maudrich. 1954.

This little volume, for the title of which there is no English equivalent, presents an accurate and succinct description of National Insurance in Austria. Written by a consultant of the great Hospital for Accidents in Vienna, and with a foreword by Professor Böhler himself, it carries unquestioned authority. It deserves the close study of all those, whether medical men or administrators, who have to deal with both health and accident insurance in this country.

Professor Böhler points out the immense importance of accuracy in both diagnosis and prognosis in insurance, the necessity for special training and experience in those who undertake the work, and the lamentable results which may follow if a mistake is made. Dr. Mayr, who was himself a general practitioner before he became consultant to the Accident Clinic, stresses the importance of an appreciation of these problems in general practice and of early recognition of conditions which may at this stage be easily corrected.

The first section describes the general organization of the clinic, which deals with some 50,000 cases each year, and gives an account of the provisions for compensation by the State. The second section, occupying two-thirds of the book, considers in detail all the conditions which may arise as the result of accidents to any part of the body. It is well illustrated and typical cases are clearly described. It concludes with a series of diagrams of possible injuries to the fingers, with a note in each case of the accepted percentage disability, which might well be adopted by our own Ministry of National Insurance and which would be of great assistance to both medical and appeal tribunals.

HENRY SOUTTAR.

A MYCOLOGICAL ATLAS

Practical Mycology: Manual for Identification of Fungi. By Sigurd Funder. (Pp. 146; illustrated. No price.) Oslo: Brøggers Boktrykkeris Forlag. 1954.

This little book, fairly described as a manual for the identification of fungi, is proffered as an introduction to mycology for beginners. It is in fact a mycological atlas comprising a large collection of excellent line drawings illustrating the characteristic microscopic morphology of various genera of fungi, with the minimum of textual description.

A short introductory section deals briefly with the fundamentals of mycology, the basis of classification, and elementary laboratory methods. The major part of the book, consisting of drawings of microscopical preparations designed as an aid in the identification of the fungi, is divided into three sections. The largest of these deals with fungi of general interest, the other two being devoted respectively to fungi of importance to the plant pathologist and those of medical interest; to the last section is appended a useful dichotomous key to the human mycoses. A schematic classification of 122 genera of the *Thallophyta* and a short glossary of mycological terms complete the volume.

As a textbook this work is wanting in balance. The admirable collection of plates for the identification of fungi will prove valuable to those with a basic knowledge of mycology, but to the beginner it is not an adequate introduction.

J. T. DUNCAN.

ATHEROSCLEROSIS

Experimental Atherosclerosis. By Louis N. Katz, M.D., and Jeremiah Stamler, M.D. (Pp. 375; illustrated. 75s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953.

It is remarkable how much information is gathered together, reassembled, and presented in logical sequence in this relatively short book of 291 reading pages. Appended are 713 references complete with titles. The authors have collected a vast amount of sifted evidence, to which they themselves have contributed in no small measure, in support of their proposition that altered cholesterol–lipid–lipoprotein metabolism plays a key role in human atherogenesis. The book is necessarily concise, well written, and therefore easily read, suitably illustrated to clarify the text, and full of detailed fact. It is strongly recommended to all workers in this important field, and will surely prove a milestone, if not a half-way house, on the road to full understanding of atherosclerosis and its consequences.

PAUL WOOD.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY APRIL 9 1955

NORADRENALINE

In 1946 the work of U. S. von Euler[1] drew attention to this very close relation of adrenaline. A substance which by its properties was indistinguishable from noradrenaline was found in the spleen, the heart, and the nerves of the sympathetic chain, and, when Tullar[2] separated the optical isomers of the synthetic compound, it was finally identified as L-noradrenaline. Von Euler put forward the view that noradrenaline was the chemical transmitter of sympathetic nerve impulses, and was in 1949 shown to be correct by Peart,[3] who demonstrated that noradrenaline was liberated in the blood when the sympathetic nerves to the spleen of the cat were stimulated.

Noradrenaline has been used clinically to restore the blood pressure in various conditions, for which purpose it is superior to adrenaline primarily because noradrenaline does not accelerate the heart. This is the consequence of its greater pressor effect, which causes by reflex action an increased vagal tone. The greater pressor action of noradrenaline is explained by the fact that it constricts the vessels in the muscles as well as those in the skin and viscera, whereas adrenaline dilates those in the muscles. The properties of noradrenaline therefore enable it to be given by an intravenous drip so that its effect is always under control and can be increased or diminished at will. So readily indeed does the blood pressure respond to an increase or a decrease in the rate of inflow of noradrenaline that, when it is given, a constant watch on the blood pressure must be kept. The other precaution is that, once an infusion of noradrenaline has been started, it should not be terminated abruptly, since the blood pressure may then fall. This is because noradrenaline, like adrenaline, depresses the transmission through the sympathetic ganglia of the impulses which maintain vascular tone, and before the infusion of noradrenaline is finally stopped the transmission must be given time to recover. Noradrenaline infusions have been used to maintain the blood pressure during the operation of removing an adrenal medullary tumour and also in the treatment of shock following cardiac infarction. Shirley Smith and Guz[4] described its use in six patients in whom the systolic blood pressure had fallen to levels between 45 and 80 mm. and who seemed about to die. In each there was prompt clinical improvement, and, though two who had had previous infarctions died within three and four days, the others recovered well, and the lives of three were saved by the treatment.

The current interest in noradrenaline concerns the purpose of its release from the adrenal gland. Vogt[5] has determined the presence of noradrenaline in the plasma of the adrenal vein of the cat, when the gland has been denervated previously. She found a mean secretion of 34 mμg. of noradrenaline per minute, compared with 21 of adrenaline. In the normally innervated gland Duner[6] has found that about three times as much noradrenaline is secreted. What is the purpose of this secretion? Does noradrenaline have a special function of its own, or is this simply the overflow of noradrenaline which is synthesized but cannot be stored? The work of West and his colleagues[7] has shown that in foetal and neonatal life noradrenaline greatly predominates both in the rabbit and in man and that very little adrenaline is present. Later the position is reversed. Hence, ontogenetically, adrenaline seems to replace noradrenaline, and therefore phylogenetically adrenaline can be regarded as a more efficient form of noradrenaline. In the blue whale there is very little adrenaline. Since Bülbring[8] has shown that noradrenaline is the precursor of adrenaline, the noradrenaline found in the adrenal vein may be the secretion of an unwanted product.

Comparisons between the amounts of noradrenaline and adrenaline in the adrenal vein during rest and activity have shown that the relative amounts change. Thus von Brücke and his colleagues[9] found that the percentage of adrenaline was raised by stimulating areas in the hypothalamus. Von Euler and Folkow[10] likewise found that the percentage of adrenaline was much greater following stimulation of the central end of the sciatic nerve or of the brachial plexus than it was when the carotid arteries were clamped. Finally, Folkow and von Euler[11] have published evidence that the proportion of the two substances in the adrenal vein can be modified by stimulating different points in the hypothalamus. Stimulation of one point caused a rise in the output of noradrenaline without raising the output of adrenaline, while stimulation of a different point caused a rise in the output of adrenaline and little or no effect on that of noradrenaline.

[1] v. Euler, U. S., *Acta physiol. scand.*, 1946, **11**, 168.
[2] Tullar, B. F., *J. Amer. chem. Soc.*, 1948, **70**, 2067.
[3] Peart, W. S., *J. Physiol.*, 1949, **108**, 491.
[4] Smith, K. S., and Guz, A., *British Medical Journal*, 1953, **2**, 1341.
[5] Vogt, M., *Brit. J. Pharmacol.*, 1952, **7**, 327.
[6] Duner, H., *Acta physiol. scand.*, 1954, **32**, 63.
[7] West, G. B., *et al.*, *Clin. Sci.*, 1953, **12**, 317.
[8] Bülbring, E., *Brit. J. Pharmacol.*, 1949, **4**, 234.
[9] Brücke, F. v., *et al.*, *Arch. int. Pharmacodyn.*, 1952, **88**, 407.
[10] v. Euler, U. S., and Folkow, B., *Arch. exp. Path. Pharmak.*, 1953, **219**, 242.
[11] Folkow, B., and v. Euler, U. S., *Circulation Research*, 1954, **2**, 191.
[12] Eränkö, O., *Nature (Lond.)*, 1955, **175**, 88.

They conclude that in the adrenal medulla there are separate cells for producing adrenaline and noradrenaline and that these are innervated by separate fibres with a different hypothalamic representation.

Eränkö[12] has used histochemical methods which reveal brightly fluorescing cell groups in the adrenal medulla; and he has shown that, when different species are examined, the percentage of the medulla occupied by fluorescing cells is very similar to the percentage of noradrenaline in the mixture of the two amines. To establish the connexion between fluorescing cells and noradrenaline more securely, Eränkö adopted the following ingenious procedure. He cut serial sections of fresh frozen glands of the cat and the hamster. Alternate sections were examined histologically for the distribution of the fluorescing islets, and the other sections were freeze-dried. He then picked out of these freeze-dried sections the pieces which the histological examination had shown to contain many fluorescent islets, and found them to contain more noradrenaline than the pieces from the same section which contained fewer fluorescing cells. Eränkö also tested the effect of injecting rats with insulin and with nicotine. He found that insulin caused a selective depletion of adrenaline and a disappearance of the chromaffin reaction from all but some cells which form islets similar to the fluorescing islets. The fluorescence of these islets was not affected by insulin. This observation agrees with the previous evidence that in insulin hypoglycaemia there is a predominant release of adrenaline. On the other hand, when Eränkö injected nicotine there was a selective loss of noradrenaline and a disappearance of fluorescing and chromaffin material from the islet cells. These observations, made possible by the methods worked out in the Department of Pharmacology in Edinburgh, constitute an important advance in our knowledge of the physiology of the adrenal medulla.

CASTRATION OF SEX OFFENDERS

Castration has been used as a form of treatment or punishment for sex offenders since at least 1500 B.C., and continues to arouse controversy. Some consider it to be a barbaric and primitive custom; its modern advocates can claim that the real effects are rarely studied impartially and that it offers an alternative to years of imprisonment. Surprisingly little is known about the effect of castration on normal human males. Castration before puberty leads to serious diminution in sexual responsiveness, but when performed after puberty the only certainty is that the effects are very variable. Beech[1] points out that "the literature is replete with references to complete retention of sexual function in individuals who have been castrated for many years," but that nevertheless the human male usually experiences a gradual loss of mating ability. Kinsey[2] questions whether this gradual loss is not largely due to the effects of advancing age, which his own studies have revealed in detail for the first time, since many of the reports do not give the age of the castrates. Most reports have failed to give detailed information, perhaps because the truth is hard to come by. Lange[3] found that victims of accidental castration exaggerated the ill effects in order to obtain financial compensation, and Stürup that castrated sex offenders are apt to boast about their potency, at least for a time. However, some types of medical treatment have been found effective even when their rationale is rather suspect, and this may be so of castration. The cautious programme carried out at the Herstedvester psychopathic prison in Denmark is much more fully described than others and deserves careful study.[4–6]

Danish law permits treatment in a special institution of sexually abnormal and other offenders who are not certifiable as psychotic or mentally defective but are not amenable to punishment. The detention is for an indefinite period. Sex offenders, selected after careful study, may be offered the opportunity of volunteering for castration; if so, they are usually released in about six months, although they remain under supervision of the institution. Some 190 offenders were castrated in the ten years after the treatment became legal in 1935. Few are said to resent or to regret it afterwards, and some who establish themselves socially are pleased with the results. Any judgment of the effects is made difficult by the low rate of recidivism of sex crimes and the great variety of offences and of personality in the offenders. In a 10-year survey of over 3,000 sex offenders in Denmark[6] the rate of recidivism for sex offenders in general was 16.8%. Except in incest cases 70–80% of the recidivism is homologous (the same sex offence). The highest rates of recidivism are for exhibitionism (32.4%), indecent assaults on boys (27.9%), and rape (22.3%). Analysed by personality, if the cause of any sex offence was considered to be "psychopathy," the recidivism was 37.6%, and, if "sexual abnormality," was 61.1%. Castration is never carried out for social convenience or security alone, but only in cases of severe but non-certifiable mental abnormality virtually untreatable by other means, and when the offences have been serious and the prognosis is bad. Thus 13.8% of men convicted of rape were castrated, 14.3% of those

[1] Beach, F. A., *Hormones and Behaviour*, 1948, New York.
[2] Kinsey, A. C., *et al.*, *Sexual Behaviour in the Human Female*, 1953, Philadelphia.
[3] Lange, J., *Die Folgen der Entmannung erwachsener an der Hand der Kriegerfahrungen dargestellt*, 1934, Leipzig.
[4] Stürup, G. K., *Acta psychiat., neurol. scand.*, 1946, **21**, 781.
[5] —— Report of Scandinavian Psychiatric Congress, 1946.
[6] —— *Int. Review of Criminal Policy*, No. 4, 1953, H.M.S.O.

committing indecent assault on boys, but only 2% of the much larger numbers committing indecent assaults on women and girls, for whom the prognosis is much better. Among 500 criminals admitted to Herstedvester before 1948, 199 were sex offenders (apparently about 2.5% of all sex offenders). Of these, 175 have been released, 117 after castration and 58 without castration; 15 are dead or in mental hospitals; 9 are still detained. Of the 117 castrated and released, only 5 have again committed a sex offence in a period of 4–10 years. Of the 58 who were released without being castrated, 25 again committed the same kind of offence. Seventeen of these later consented to be castrated and were released; so far they have not been convicted of further offences. Thus a total of 134 have been released after castration, with a homologous recidivism of 3.7%. Perhaps the most interesting feature is that all the 5 men who committed a sex offence after castration were homosexuals who associated with boys. Thus the recidivism for castrated heterosexuals was nil, but was about 10% for the 49 homosexuals who were castrated. The homosexual's attitude to castration may be more complex, and his opportunity for legitimate expression more limited, though homosexual activity between adults is not an offence in Denmark. The castrated and non-castrated groups, however, are not strictly comparable, since there is a natural tendency to risk releasing the minor offenders, such as exhibitionists, and to detain—sometimes for 10–15 years—men convicted of rape who refuse castration.

In Britain there are probably few advocates for the castration of sex offenders; and the Danish results, impressive as they are, do not suggest that castration offers such a sound solution to the problem of treating these people that we should re-examine the basis of our reluctance to use it. Nevertheless the more frequent passing of sentences of up to fourteen years' preventive detention may stimulate a humanitarian demand for some alternative to imprisonment. The production of reversible castration by means of oestrogens, perhaps implanted, might be worth studying.

PURE RED-CELL ANAEMIA

Marrow hypoplasia or aplasia is now known to affect haemopoiesis in more than one way. In what might be called typical aplastic anaemia the hypoplasia affects the formation of leucocytes and platelets as well as red cells and gives rise to pancytopenia in the peripheral blood. Less commonly, the formation of red cells is seriously affected and leads to a profound reticulocytopenia, although the production of leucocytes and platelets continues normally or almost normally. This latter type of anaemia—pure red-cell anaemia[1]—gives rise to several distinct clinical entities. The first of these is a chronic anaemia in infants—congenital hypoplastic anaemia[2] or erythrogenesis imperfecta.[3] The second is an acquired chronic anaemia in adults—sometimes apparently associated with tumours of the thymus.[4,5] And thirdly a temporary condition occurs occasionally in the course of congenital haemolytic anaemias[6–8] and rarely in auto-immune acquired haemolytic anaemia[9,10] or in previously healthy children.[7]

Pure red-cell anaemia of infants is usually diagnosed in the first year of life, though the infant may appear healthy at birth. Anaemia is the sole symptom and the children develop normally as a rule. The most striking pathological feature is the virtual or perhaps complete absence from the marrow of the nucleated precursors of the red cells. Nothing certain is known of the cause of the disorder. Recently, however, K. I. Altman and G. Miller[11] have demonstrated anthranilic acid in the urine of several children suffering from pure red-cell anaemia; this suggests an abnormality in tryptophan metabolism, but the link between the abnormality and the anaemia remains obscure. Periodic transfusion is usually necessary, and the outlook for the patient is rather grave. Even so, spontaneous cure or substantial improvement has been reported. Some of these children have been treated with A.C.T.H. or cortisone, or by splenectomy, or both. The results seem unpredictable and usually unsatisfactory.[3,12]

It is uncertain what relationship there is, if any, between the pure red-cell anaemia of infancy and typical aplastic anaemia leading to pancytopenia. Moderate degrees of leucopenia have been observed in children who otherwise would seem to belong to the group of pure red-cell anaemia.[13] A further complication is the finding of peripheral reticulocytopenia (with normal leucocytes and platelets) in children whose marrows show normal or even increased numbers of erythroblasts instead of the expected hypoplasia. In these patients arrest of maturation rather than red-cell aplasia seems to be the cause of the anaemia.[14]

Pure red-cell anaemia in adults is a rare disease, and the pathogenesis is uncertain. In at least nine patients a tumour of the thymus (usually a benign thymoma) has been associated with the anaemia; some but not all of the patients have had myasthenia gravis.[4,5] The case histories recently reported by Drs. J. N. M. Chalmers and K. Boheimer in this *Journal*[4] are particularly interesting. The first patient developed temporary remissions following, respectively, thymectomy and splenectomy, and later went into apparent permanent remission after

[1] Lescher, F. G., and Hubble, D., *Quart. J. Med.*, 1932, **25**, 425.
[2] Diamond, L. K., and Blackfan, K. D., *Amer. J. Dis. Child.*, 1938, **56**, 464.
[3] Cathie, I. A. B., *Arch. Dis. Childh.*, 1950, **25**, 313.
[4] Chalmers, J. N. M., and Boheimer, K., *British Medical Journal*, 1954, **2**, 1514.
[5] Ross, J. F., *et al.*, *Blood*, 1954, **9**, 935.
[6] Owren, P. A., ibid., 1948, **3**, 231.
[7] Gasser, C., *Sang*, 1950, **21**, 237.
[8] Singer, K., *et al.*, *J. Lab. clin. Med.*, 1950, **35**, 721.
[9] Davis, L. J., *et al.*, *Glasg. med. J.*, 1952, **33**, 263.
[10] Eisemann, G., and Dameshek, W., *New Engl. J. Med.*, 1954, **251**, 1044.
[11] Altman, K. I., and Miller, G., *Nature, Lond.*, 1953, **172**, 868.
[12] Smith, C. H., *J. Pediat.*, 1953, **43**, 457.
[13] Palmen, K., and Vahlquist, B., *Acta haemat.*, 1950, **4**, 273.
[14] Bernard, J., *et al.*, *Sem. hôp. Paris*, 1951, **27**, 2985.
[15] Loeb, V., *et al.*, *Amer. J. Med.*, 1953, **15**, 499.
[16] Foy, H., and Kondi, A., *J. Path. Bact.*, 1953, **65**, 559.
[17] Seaman, A. J., and Koler, R. D., *Acta haemat.*, 1953, **9**, 153.
[18] Fountain, J. R., and Dales, M., *Lancet*, 1955, **1**, 541.

receiving a course of A.C.T.H.; the second patient responded similarly to A.C.T.H. after thymectomy and splenectomy, which in themselves had conferred little or no benefit. Two other patients referred to by Chalmers and Boheimer responded to thymectomy (without splenectomy or A.C.T.H. therapy), but in neither of the patients of Ross and co-workers[5] was the operation successful. Chalmers and Boheimer suggest that the anaemia may be brought about by an inhibitor of erythropoiesis, formed in lymphoid tissue, and that thymectomy may be successful, depending upon the degree of interference with erythropoiesis. In Chalmers and Boheimer's own patients, on this hypothesis, removal of the spleen as well as the thymus did not remove sufficient lymphoid tissue for erythropoiesis to proceed; only after subsequent A.C.T.H. therapy, which perhaps caused a further depression of lymphoid tissue, did erythropoiesis take place normally. In those cases, too, in which a similar type of anaemia has occurred with no evidence of a thymic tumour remission has followed splenectomy with or without subsequent A.C.T.H. or cortisone therapy.[15] Finally, it should be mentioned that patients suffering from pure red-cell anaemia have been recorded as responding to riboflavine[16] and cobalt.[17 18]

The concept of inhibition of erythropoiesis resulting from hyperplasia of lymphoid tissue is especially interesting. The spleen had often been thought capable of inhibiting haemopoiesis; usually, however, the result of "hypersplenism" is pancytopenia. The case reported by G. Eisemann and W. Dameshek,[10] in which red-cell hypoplasia associated with an auto-immune haemolytic anaemia disappeared following splenectomy, might be looked upon as an example of a more specific type of hypersplenic activity.

SEASONAL INCIDENCE OF PEPTIC ULCER

It has long been a clinical impression that the symptoms of gastric and duodenal ulcers are exacerbated in the spring and autumn. If they are, the fact is of considerable theoretical interest, for it may provide a clue to the aetiology of two conditions which at present eludes us. Few objective data support the impression, and they are not altogether consistent. The subject is reviewed by A. C. Ivy, M. I. Grossman, and W. H. Bachrach.[19] Data for the month of onset of pain, haemorrhage, perforation, and death all show a decreased incidence in summer and a sharply increased incidence in the late autumn or winter. Most data have been obtained from the northern hemisphere, but the same rhythm has also been shown to exist—so far as symptoms are concerned—in the southern hemisphere.[20] Some data suggest that there may also be an increase of activity in the spring, but the evidence for this is not striking. In fact, R. A. Jamieson,[21] who studied the distribution of nearly 8,000 cases of acute perforation treated in the three main Glasgow hospitals, found that throughout this period of the year the incidence was remarkably constant. A partial explanation of these differences may perhaps be found in the grouping together of cases of gastric and duodenal ulcer. According to R. S. Boles and M. P. Westerman,[22] who have recently reported on 320 cases of peptic ulcer admitted for haemorrhage to the Philadelphia General Hospital over the five years 1949–53, the peak months for gastric ulcer admissions were between January and June, with a lower incidence in the late summer and the autumn; while duodenal ulcer admissions showed two peaks of incidence, one in March and the other in November, with a minimum in July. Boles and Westerman suggest that the pattern for duodenal ulcer may be related to changes of temperature—the peaks of incidence occurring in the months in which the extent of the change between the beginning and end of the month is the greatest. They also suggest—though they provide no data in support—that haemorrhage may be precipitated by changes in barometric pressure. The correlation shown between temperature change and incidence of haemorrhage is undoubtedly close over the latter half of the year, but it is much less striking during the first six months, and, if their explanation were to be accepted, it would be necessary to postulate some additional factor responsible for the relatively high incidence in the middle of the winter. Other explanations put forward in the past are that the activity of an ulcer may be stimulated by upper respiratory infections or by the ingestion of vegetables which are subject to seasonal fluctuation in their supply. These suggestions, though stimulating to research, are based on very little factual data, and it may well prove that Jamieson was right in concluding that, so far as perforations are concerned, the decrease in incidence between mid-July and October is due to the physical rest associated with holidays and comparable to the reduced incidence characteristic of Sundays and Mondays and of the early hours of the morning.

[19] Ivy, A. C., *et al.*, *Peptic Ulcer*, 1950, London.
[20] Linn, H., *Med. J. Aust.*, 1946, **2**, 649.
[21] Jamieson, R. A., *British Medical Journal*, 1947, **2**, 289.
[22] Boles, R. S., and Westerman, M. P., *J. Amer. med. Ass.*, 1954, **156**, 1379.

THIS YEAR'S BILL

An increase of some £25m. in the total cost of the Health Service in 1955–6 had already been foreshadowed in the Vote on Account published a few weeks ago. The detailed estimates[1] that have now appeared show how the increase is distributed among the different branches of the Service.

The interesting thing is that each main branch shows an increase of some sort, though where the cost is partly offset by patients' payments—in the pharmaceutical, dental, and supplementary ophthalmic services—the net increases, after allowing for these payments, look insignificant against a background of £462m. being spent on the Service as a whole. But, small as they are, they give the impression that the effect of the charges has to a certain extent worked itself out. The gross cost of dental treatment is still well below the peak it reached in the early years of the Health Service—when dentists' fees were higher. But at £35½m. (reduced by charges to patients to £27½m.) it has climbed some way from the

[1] *Civil Estimates for the Year Ending March* 31, 1956, Class V. H.M.S.O., 6s.

low level it fell to when the charges were first introduced. A similar trend can be observed in the cost of the ophthalmic service. As regards the pharmaceutical service, a year ago the estimate (for 1954–5) was much the same as for the previous year, and there seemed some hope that a combination of charges and exhortations to doctors to prescribe economically had stabilized the cost of this service, which had gone up inexorably since 1948. But in the event a supplementary estimate of some £2m. was needed in the course of the year, and this year's estimate, though only slightly higher at £55m. gross (and £47½m. net), is £7m. higher than the estimate for the year when the shilling charge was introduced.

In all these cases the rise in the estimates reflects a bigger demand by the public rather than a rise in the cost of providing the Service, though drugs are certainly no cheaper. So far as the hospitals are concerned, the increase in the estimated advances to boards is largely accounted for by higher salaries and wages and other maintenance costs. The recent award to nurses was estimated to cost over £4m. a year, and in this instance there are expected to be more staff to pay, for 8,000 more nurses and midwives are now being employed than a year ago. The number of consultant and other medical staff, on the other hand, is roughly the same. On the whole, however, this year's estimated rise of nearly £20m. in the cost of maintaining the hospitals is due to the higher cost of the existing service rather than to any noticeable expansion. That will not come until the new hospital building programme, announced earlier this year to start in 1956–7, has been completed. But long before that the Guillebaud committee on the cost of the Health Service will have reported, and—just possibly—some change in the method of financing the hospitals may have been introduced.

CEREBRAL BASIS OF MEMORY

The relationship of mind and brain remains as firmly established and its exact nature as obscure as in the days of the Hippocratic school. The question has been of perennial interest to neurologists, and within the last few decades they have been able to throw light on the more limited problem of which parts of the brain especially influence consciousness. While Pavlov's view of the cerebral cortex as an analyser and therefore an essential organ for fine discriminatory consciousness remains unassailed, recent interest has focused on the neural background of the more crude diffuse "awareness" that must lie behind discrimination. The occurrence of pathological sleep in man in encephalitis lethargica with lesions shown to be maximal in the hypothalamic region, and later Hess's[1] production of sleep by electrical stimulation of limited sites in the diencephalon of animals, both directed attention to subcortical structures. The late Sir Hugh Cairns, in his Victor Horsley lecture,[2] reviewed the evidence, from his own considerable experience, for a causal connexion between disturbances of consciousness and lesions of the brain stem and diencephalon. He concluded that such lesions could produce "severe disturbance of consciousness which arises without any direct involvement of the cortex or corticospinal pathways," and suggested that the reticular formation was an important part of the anatomical background for this.

Cairns's interest in this field has been maintained by his colleagues in the Oxford Medical School, and Williams and Pennybacker[3] have made a valuable study of disturbance of memory in patients with brain tumours involving the floor and sides of the third ventricle. All of their four cases showed a Korsakov type of memory defect—amnesia with confabulation (that is, answering questions and recounting experiences without regard to actual happenings). In one the relation of symptoms to the function of third ventricular grey matter seemed particularly well established, because a cystic tumour which pressed on these structures was present: when the pressure was relieved by evacuation of the cyst symptoms subsided, only to recur as the cyst again filled up. The authors provide convincing collateral evidence that the memory disturbances were not associated with other and more diffuse cerebral lesions or with such factors as raised intracranial pressure. The quality of the memory defects was of special interest. Usually they were accompanied by some reduction in responsiveness and alertness, though the general dementia seen in other cerebral lesions was not present. But the striking feature was the confabulation and pseudo-reminiscence produced by attempts at recalling memories: it was almost as if the content of memory was still there but that its orderly arrangement and temporal sequence were at fault. In this sense the disturbances seem to follow the diffuse rather than discriminatory pattern of other subcortical lesions. A study[4] of the mental disturbances in tuberculous meningitis is also concerned with defects of memory. In some patients such defects were prominent, consisting especially of "an inability to organize past events in correct temporal sequence"; and in these cases also the inflammatory process directly involved the floor of the third ventricle. The authors are cautious in connecting the two observations, but their evidence for a causal relation seems convincing and confirmatory of other work.

[1] *Das Zwischenhirn*, 1949. Basel.
[2] *Brain*, 1952, **75**, 109.
[3] *J. Neurol. Neurosurg. Psychiat.*, 1954, **17**, 115.
[4] Williams, M., and Smith, H. V., ibid., 1954, **17**, 173.

SUCROSURIA

Not so long ago "marasmus" was a term used to cover ignorance about the reasons why certain infants did not thrive after birth. Modern diagnostic methods, in particular chromatography, have shown that these infants may suffer from serious metabolic disorders, and it should be accepted that any child with obscure wasting requires urgent and specialized investigation. In this way, for example, Moncrieff and Wilkinson[1]—writing in a special number of *Acta Paediatrica* in honour of Professor A. Wallgren's 65th birthday—have recently discovered sucrose in the urine of three such

[1] *Acta paediat. (Uppsala)*, 1954, **43**, Suppl. 100, p. 495.

patients. Sucrose is a disaccharide which, unlike other common sugars, does not reduce alkaline copper reagents. It is rapidly split by hydrolysis in the intestine—probably by a combined action of gastric juice and succus entericus—into its component sugars, glucose and fructose, which pass quickly to the liver. If sucrose escapes hydrolysis it enters the tissue fluids, where it behaves as an inert substance and is excreted by the kidneys. Because of its rapid absorption this particular sugar is often used in the treatment of hypoglycaemia. Its presence in the urine has occasionally been reported in patients with gastro-intestinal and pancreatic disorders.

Studies by paper chromatography show that most sugars are excreted in small quantities in the urine of infants. In Moncrieff and Wilkinson's cases, however, abnormal amounts of fructose, lactose, and sucrose appeared after milk feeds (which contain lactose and sucrose). A single dose of sucrose increased the abnormality. When various combinations of dietary sugars were fed to the infants it was possible to recover individual sugars from the urine provided that sucrose and lactose were present in the diet. Moncrieff and Wilkinson are not yet able to say what is the nature of the defect in carbohydrate metabolism in their patients. Attempts to measure the activity of succus entericus were not wholly successful, but the fact that fructose was excreted after a dose of sucrose suggests that splitting takes place in the intestine. There must, however, be very rapid absorption before hydrolysis is complete, and it is significant that both sucrose and lactose are disaccharides, which perhaps compete with each other for hydrolysis. More will be learned about the utilization, storage, and excretion of sugars when further cases of this abnormality are detected. All three infants suffered from mental defect and hiatus hernia in addition to the sucrosuria. It is not clear whether these are associated congenital lesions or whether they are closely related to the sucrosuria. Necropsy in one infant showed developmental abnormalities in the brain, and it is difficult to imagine a relationship between an oesophageal lesion and abnormal sugar metabolism. On the other hand, galactosaemia is known to result in mental retardation. The fact that two infants died and the third is mentally and physically backward makes it unnecessary to stress the need for early detection of this interesting new metabolic error.

ELECTRICAL ACTIVITY OF THE UTERUS IN LABOUR

During the last few years interest has been shown in the recording of the electrical activity of the human uterus during labour.[1-3] In a recent paper C. M. Steer[4] has reviewed his findings in 556 parturient women in whom recordings were made with his electro-hysterograph (E.H.G.). The value of this review is enhanced by the fact that the E.H.G. findings were not allowed to influence the management of any case, nor were they used to classify a labour as normal or abnormal. The E.H.G. is a device employing three pairs of electrodes placed on the abdominal wall so that one pair lies over the right uterine cornu, another correspondingly on the left, and the third over the midline of the fundus. The location, duration, frequency, and amplitude of the electrical waves can thus be recorded. The waves are present only during uterine contractions, whether of true or false labour at or before term, and between contractions there is a relatively smooth tracing in which the electrocardiogram can usually be seen. The wave of electrical activity begins simultaneously with the mechanical contraction, some 10–20 seconds before pain is appreciated; the electrical wave and the pain end simultaneously, at which time relaxation begins, to become complete in a further 15–30 seconds. In normal labour the frequency of the waves is ½–2 cycles per minute, while the amplitude varies from 50 to 500 microvolts in direct proportion to the clinical strength of the uterine contractions.

Steer considered in particular detail 51 labours, all but two in primigravidae, in which a clinical diagnosis of uterine inertia was made. Such a diagnosis was based on the failure of the cervix progressively to dilate, with the strength and frequency of contractions remaining unchanged or becoming weaker. The eventual duration of labour varied from 15 to 120 hours with a mean and median of 35 hours. The significant finding by E.H.G. was the absence of electrical activity during contractions in five of these 51 women. Two of the five were treated with pitocin by intravenous drip, while in the other three only sedative and supportive measures were employed; but in all five cervical dilatation never progressed beyond two fingerbreadths, and caesarean section was required. In Steer's opinion these are cases of true primary uterine inertia, and he remarks, as others have done, that this is a rare condition. In the remaining 46 women electrical activity was present, and Steer regards these as cases of slow but basically normal labour, in which stimulation with pitocin is nearly always effective. He notes, however, that disproportion was present in over one-third of these 46 cases. The importance of such coexistence of disproportion and inertia, an association which again has been remarked by others, lies in the fact that stimulation with pitocin may succeed in overcoming minor disproportion and effecting vaginal delivery, but only at the cost of damage to the foetus.

The electro-hysterograph can thus serve to distinguish between the more common slow normal labour and the rarer true inertia which represents some basic disturbance of uterine muscle activity. Such a distinction can also be made by observing the results of stimulation with pitocin, but without the same absolute safety. The nature of true inertia is still unexplained. The uterine muscle contracts but does not provide sufficient force for progressive labour, and Steer concludes by suggesting that the fault may lie either in the contractile apparatus within the uterine muscle fibre or in the transmission of the impulse to contract.

[1] Steer, C. M., and Hertsch, G. J., *Amer. J. Obstet. Gynec.*, 1950, **59**, 25.
[2] Halliday, E. C., and Heyns, O. S., *J. Obstet. Gynaec. Brit. Emp.*, 1952, **59**, 309.
[3] Lévy-Solal, E., *et al.*, *Presse méd.*, 1952, **60**, 1335.
[4] Steer, C. M., *Amer. J. Obstet. Gynec.*, 1954, **68**, 867.

EMERGENCIES IN GENERAL PRACTICE

DIABETIC AND INSULIN COMA

BY

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The treatment of severe diabetes mellitus involves the use of one or more of the many insulin preparations now available and the prescription of a suitable diet. There is an increasing tendency for the routine management of these patients to be undertaken in special hospital out-patient clinics, partly because in some cases it is difficult and time-consuming, and partly because the help of dietitians and other ancillary workers may be required. The general practitioner is apt to see his diabetic patients only if some emergency arises, such as an intercurrent infection or the development of ketosis or severe hypoglycaemia. When this happens, lack of familiarity with the patient's diabetic condition makes his task much harder.

Diabetic Coma and Pre-coma

It is now generally accepted that diabetics fall broadly into two groups—those who are underweight and those who are overweight when the condition is recognized. It seems likely that in the first type insulin-lack is the underlying cause, whereas in the second type insulin is still being produced by the pancreas in approximately normal amounts. Both groups have a high blood sugar with glycosuria and polyuria, but those suffering from insulin lack tend, in addition, to produce an excess of ketone bodies unless adequate replacement therapy is given. If these ketone bodies are being formed so fast that they accumulate in the blood, the patient may be said to be in a state of diabetic ketosis, and unless treatment is given will deteriorate, first becoming drowsy and finally unconscious. Coma resulting from severe diabetic ketosis is fortunately rarely seen nowadays, and the practitioner is concerned with recognizing the condition in the pre-coma stage, which in itself is to be regarded as a medical emergency.

Severe diabetic ketosis or diabetic pre-coma is usually defined on a biochemical basis (carbon dioxide combining power less than 20 vols.%), but on clinical assessment it may be said to be present when, following a period of severe diabetic imbalance, there is evidence of dehydration and the patient's breath smells strongly of acetone. In this condition there is a heavy glycosuria and in almost all cases ketone bodies are present in sufficient concentration to give a positive ferric chloride reaction.

Patients with recently developed diabetes rarely reach the stage of severe ketosis before seeking medical advice. Known diabetics may go into ketosis because the dose of insulin prescribed for them is inadequate or because their syringe is defective and they are not getting the full amount. Much more commonly it follows a sudden increase of insulin requirement produced by an intercurrent infection, usually of the upper respiratory or gastro-intestinal tract. Occasionally an emotional upset increases the insulin requirement enough to lead to diabetic ketosis.

Recognition of Severe Diabetic Ketosis

Severe diabetic ketosis does not develop in a matter of hours: with very few exceptions the patient will give a history of thirst, polyuria, and nocturia for several days. As the ketosis becomes more severe, appetite is lost and increasing nausea is followed in many cases by vomiting. Intense thirst persists until consciousness is lost. Some patients, when they lose their appetite or start to vomit, reduce or omit their insulin injections—a step that still further aggravates their condition. Constipation is the rule and is occasionally associated with severe abdominal pain suggestive of an acute attack of appendicitis or some other surgical emergency. In a few cases the acidotic respiration is very striking and the patient's chief complaint is of breathlessness or dyspnoea.

A history of increasing thirst and polyuria followed by nausea and vomiting in a diabetic patient should warn the practitioner of the possibility of diabetic ketosis. The most important findings on physical examination are signs of dehydration—a dry red tongue, inelastic skin, and often a reduction of blood pressure. The breathing is usually very deep and may be rapid. The breath smells strongly of acetone.

Examination of the urine is of great importance, and, unless the patient is unconscious or severe dehydration and hypotension have led to impairment of renal function, there is seldom any difficulty in obtaining a specimen. This should first be tested for sugar. There is no longer any need to use Benedict's solution or to boil the urine in a test-tube over a spirit flame. The "clinitest" tablet method has been shown to be accurate and reliable and is much more convenient for use in the patient's home. If the urine contains less than 2% sugar it is extremely unlikely that the patient is in diabetic ketosis. An approximate quantitative assessment of the percentage of sugar in the urine is obtained from the colour chart provided with the tablets. Corresponding colours obtained with Benedict's test, using 0.5 ml. urine and 5 ml. reagent, are as follows:

	Clinitest Colour	Benedict Colour
0%	Blue	Blue
¼%	Yellow-green	Cloudy green
½%	Yellow-brown	Yellow
2% or more	Orange	Red

If there is a heavy glycosuria the urine should next be tested for ketones: a number of methods are available. The sodium nitroprusside or Rothera test is extremely sensitive and in practically all cases of severe diabetic ketosis it is very strongly positive. The ferric chloride test is much less sensitive and a true positive result indicates a gross ketonuria and the presence of a severe degree of ketosis. Unfortunately, however, salicylate medication leads to a false-positive reaction in the ferric chloride test and it is not uncommon for patients, feeling unwell on account of their unbalanced diabetes, to take a couple of aspirins. Methods are available for distinguishing the false-positive from the true-positive ferric chloride reaction, but these involve boiling the urine for 10 minutes and are not really suitable for use in the patient's home. Recently a tablet modification of the Rothera test has been introduced and has greatly simplified the detection of significant degrees of ketonuria. When using the "acetest" tablet a ++ or +++ reaction indicates marked ketonuria, corresponding to a true-positive ferric chloride reaction. It must be emphasized that the colour given by the acetest tablet is much weaker than that of the original Rothera test, and any patient giving a ++ or +++ result on the chart provided with the tablets should be considered to have severe diabetic ketosis and to be in urgent need of treatment.

Diagnostic Difficulties

A number of conditions have been incorrectly diagnosed as diabetic ketosis: salicylate poisoning, meningococcal meningitis, and subarachnoid haemorrhage may be quoted

as examples. Such errors are rare and may be avoided by careful consideration of the clinical features and critical assessment of the results of the urine tests. There are two situations, however, which more often give rise to difficulty.

Obese diabetics, seriously ill with cerebral or coronary thrombosis, often develop some degree of starvation ketosis. The presence of ketonuria in a drowsy or comatose diabetic may lead to the diagnosis of diabetic ketosis being made. Obese diabetics, however, do not lack insulin and are not liable to develop true diabetic ketosis. The differentiation between true diabetic ketosis and starvation ketosis occurring in a seriously ill obese diabetic is of some prognostic importance. Diabetic ketosis usually responds dramatically to suitable treatment, whereas large doses of insulin are unlikely to help the obese diabetic.

Severe diabetic ketosis may on very rare occasions be present without ketonuria. Failure to excrete the ketones is the result of secondary impairment of renal function. These patients always have oliguria. The clinical features and especially the strong smell of acetone in the breath should point to the correct diagnosis.

Prevention of Diabetic Ketosis

The practitioner is particularly concerned with the prevention of ketosis in a diabetic patient who develops an intercurrent infection. Not only must he treat the infection as intensively as possible but also ensure strict control of the diabetes. These patients should be instructed to test their urine before each meal, or, if they are not taking food, at least four times a day. If the intercurrent illness is severe, long-acting insulins (globin, protamine zinc, or insulin zinc suspension) should be discontinued and regular doses of soluble insulin given instead. One-third of the previous total dose should be given six-hourly; when calculating the dose to be taken the practitioner should ask to see both the insulin bottle and the syringe and verify the usual dose taken. This is necessary because patients often refer to marks on the syringe as units, and as most syringes are graduated for single-strength insulin, whereas that usually used is double or quadruple strength, confusion can easily arise.

If the urine tests continue to show 2% or more of sugar the insulin dose should be increased by about 10% every six hours until the urine sugar falls to 0.5% or less. When the urine is sugar-free, the insulin dose should be reduced. If the patient is unable to take food, glucose drinks should be given at a rate of about 10 g. of glucose hourly (10 g. glucose=approximately one level tablespoonful of glucose powder). If there is severe vomiting insulin should still be given based on the results of the urine tests, but if the urine sugar falls below 2% while there is a heavy ketonuria (++ or +++ with acetest tablets) parenteral therapy is indicated and the patient should, if possible, be sent into hospital. If the intercurrent infection is only mild the patient's usual insulin may be continued, but if there is 2% of sugar in the early morning urine the dose should be increased by 10% (patients using protamine zinc insulin alone or insulin zinc suspension should increase the dose by 20%) and further tests taken before each meal. If 2% glycosuria continues an additional small dose of soluble insulin should be given before meals and at bedtime.

The method of control outlined for these patients is only applicable if the renal threshold for glucose is normal. Some diabetics have an abnormally low threshold and pass sugar in the urine, sometimes up to 2%, while their blood sugar is in the normal range. Patients soon discover if they have this abnormality, and know that for them a sugar-free urine is a warning of impending hypoglycaemia. In these cases the best indication that an increase of insulin dose is needed is the presence of thirst and polyuria, but, if the intercurrent infection is at all severe, blood-sugar estimations are likely to be needed and admission to hospital should be advised.

Emergency Treatment of Severe Diabetic Ketosis

Severe diabetic ketosis requires hospital treatment, and this is essential if there is dehydration associated with nausea or vomiting. Furthermore, experience has shown that a delay of even a few hours may influence the ultimate outcome, therefore the practitioner should initiate treatment before leaving the patient's home. Every practitioner should have a supply of soluble insulin (80 units per ml. strength) and of sterile ampoules of 50% glucose solution, so that he can take them on any emergency call to a diabetic patient. In severe diabetic ketosis soluble insulin in large doses is required, and if the practitioner is certain of the diagnosis he should give 50 to 100 units by deep intramuscular injection. A dose of 100 units is to be regarded as the standard for a case of severe ketosis with dehydration, nausea, and vomiting, but if the patient is a previously undiagnosed diabetic or a child the dose should not exceed 50 units.

In less severe cases without any nausea or vomiting, treatment can, when necessary, be undertaken at home. If the patient is an adult and a known diabetic, treatment should be started with a dose of 50 units of soluble insulin. At the same time fruit-flavoured saline drinks should be ordered (2.7 g. of salt—about half of a level teaspoonful of table salt—in a pint (570 ml.) of water) and given at the rate of one to two pints (half to one litre) every three hours. After the first three hours glucose should be added to the drinks, about 50 g. spread over each three-hour period. Urine tests should be made every three hours and the insulin dose repeated if the urine still contains more than 2% sugar. If the patient is unable to produce a urine specimen after three hours, it suggests that the blood sugar has been reduced to the normal range and that in consequence the glycosuria and polyuria are controlled; the next insulin dose should therefore be omitted. As the glycosuria decreases, glucose and insulin in smaller doses should be continued until the ketonuria is abolished. If the patient is responding satisfactorily to treatment a reduction of the ketonuria should be apparent by the sixth hour; if this has not been achieved or if there has been vomiting at any time in the course of treatment it is probably advisable to send the patient into hospital. The principal steps to be taken in the management of patients with diabetic ketosis treated at home are given in the following table:

Treatment of Diabetic Ketosis at Home

Note: This is not suitable for patients who are nauseated or vomiting.

On making the diagnosis give 50 units of soluble insulin intramuscularly and start fruit-flavoured saline drinks.

At 3 hours:

- Obtain a urine specimen and test for sugar and ketones.
- If urine sugar 2% give 50 units of insulin
  " " " 1% " 32 " " "
  " " " 0.5% " 16 " " "
  " " sugar-free or if no specimen obtainable omit insulin
- Add glucose to saline drinks—50 g. every three hours

At 6 hours:

- Obtain and test urine specimen
- Repeat insulin as at three hours
- Continue glucose-saline drinks. If glycosuria is 0.5% or less, milk and light diet may be started
- If there has been no improvement in the patient's condition and ketonuria, transfer to hospital is advisable

If the ketosis has been precipitated by an intercurrent infection immediate steps should be taken to treat the infection.

Hypoglycaemic or Insulin Coma

Although "insulin reactions" or mild hypoglycaemic attacks are quite common in diabetics taking insulin, severe episodes leading to coma are relatively rare. The commonest causes of insulin reactions are unusual exercise, missed and delayed meals, or a sudden alteration in the insulin requirement. The reactions resulting from physical exertion may be somewhat misleading in patients taking long-acting insulins, because, instead of occurring during or immediately after the

exercise, they tend to be delayed and to come on during the night or even the next day. Reactions due to a sudden alteration of insulin requirement may occur after an illness in which the insulin dose has had to be increased. When the patient is convalescent and resumes normal activity the insulin requirement often falls rapidly and it is difficult to judge the dose required.

Recognition of Hypoglycaemic Coma

Patients on soluble insulin usually have adequate warning that their blood sugar is falling dangerously low. Blurring of vision, slurring of speech, unsteadiness of gait, sweating, or a sense of unreality all draw attention to the need for glucose or other easily assimilated carbohydrate food. Patients using long-acting insulins may have insulin reactions following this pattern, but in some cases there may be loss of consciousness without any of the warning signs; in others the patient becomes disorientated and violent so that he fails to appreciate the situation and may refuse to take a glucose drink. Another danger with the hypoglycaemic attacks of the long-acting insulins is that they tend to come on during the night. When this happens a severe attack will result in the patient being found to be unrouseable in the morning. Mild nocturnal hypoglycaemia often leads to unpleasant nightmares, and the patient wakes the next morning drowsy, and with a headache which may be relieved by breakfast or persist through the day.

When the blood sugar falls to an unusually low level during a hypoglycaemic attack, typical epileptic convulsions may occur. In older patients with cerebral vascular disease Jacksonian fits and hemiplegia may result from mild hypoglycaemia.

Hypoglycaemic coma compared to diabetic coma is a condition of rapid onset. The patient is seen going about his business and apparently quite well, and then half an hour later he is found unconscious; or he goes to bed normal in the evening and the next morning he cannot be roused. Further details about the case are of value in making the correct diagnosis. It is helpful to know that the patient is a diabetic taking insulin—for this reason all diabetics who take insulin should carry a card giving the details. Secondly, a knowledge of the patient's meals and activities may give a clue to the diagnosis, whether at the time the attack came on the patient was late for a meal or whether there had been some unusual physical exertion.

On examination there is usually a striking absence of physical signs. The patient, unless actually having an epileptic convulsion, appears to be sleeping quietly, breathing normally, well hydrated but pale, and sometimes sweating. In severe attacks the plantar responses may be extensor and in older patients there may be signs of a hemiplegia. Urine examination is of little value; the presence of urine in the bladder containing 2% sugar does not exclude hypoglycaemic coma, because the urine may have been secreted before the blood sugar fell, or the patient may have a low renal threshold. In some cases a trace of acetone may also be present.

Emergency Treatment of Hypoglycaemic Coma

Hypoglycaemia is a dangerous condition. If the nutrition of the brain is seriously affected, recovery may be delayed or never occur; after a severe episode of hypoglycaemia the patient may be dull and retarded for several months, and permanent mental defect has been described in children after repeated attacks. Immediate treatment is needed, and the best way to restore the blood sugar in an unconscious patient is to give an intravenous injection of 40 ml. of 50% glucose solution. In most cases the patient will rouse after this has been given, but after a severe attack it may be 24 hours or more before consciousness is regained. If the patient fails to respond to intravenous glucose, arrangements should be made for transfer to hospital so that continuous intravenous therapy can be given. If the patient does respond, glucose drinks should be given by mouth; this is particularly important if the attack is due to a long-acting insulin, because the patient can easily slip back into hypoglycaemic coma. A dose of 50 g. of glucose should be given at once in about 300 ml. of fruit juice, followed by a further 50 g. an hour later, or, better still, if the patient is able to take it, a normal meal.

Some of the most severe attacks have occurred when a patient found in coma due to hypoglycaemia has been incorrectly diagnosed as being in diabetic coma and given a large dose of soluble insulin. The differentiation between these two types of coma is seldom difficult—hypoglycaemia comes on rapidly or overnight, the patient is not dehydrated, and there is no smell of acetone in the breath. Coma due to diabetic ketosis follows several days of severe thirst and polyuria, and the patient is drowsy for 12 hours or more before consciousness is lost, dehydration is marked, and the breath smells strongly of acetone. If the practitioner is in any doubt, an injection of 50% glucose solution should be given; this will lead to an immediate improvement in nearly all cases of hypoglycaemia, whereas if the case is really one of diabetic coma little or no harm will result.

Next article on Emergencies in General Practice.—"Corrosive Poisoning," by Dr. J. D. P. Graham.

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ADVANCES IN CARDIOVASCULAR SURGERY

REPORT OF AN INTERNATIONAL SYMPOSIUM AT THE HENRY FORD HOSPITAL, DETROIT, MARCH 17–19

[FROM A SPECIAL CORRESPONDENT]

The outstanding contribution to this symposium was that of WALTON LILLEHEI (Minneapolis). Earlier in the programme a panel had discussed the diagnosis and treatment of congenital pulmonary stenosis, during which WILLIS POTTS (Chicago) and HELEN TAUSSIG (Baltimore) described their vast experience with the indirect or shunt operations and Sir RUSSELL BROCK (London) strongly advocated direct surgery in the form of either pulmonary valvotomy or infundibular resection; the latter even went so far as to state that in the future the treatment of the tetralogy of Fallot would be a direct operation during which each of the congenital malformations would be corrected. It was Lillehei who showed that such an operation is now a reality. He reported the results of 30 operations on patients using a controlled cross-circulation technique which allows the surgeon to open the heart widely and gives plenty of time for carefully performed intracardiac procedures under direct vision.

Septal Defects

Lillehei had confirmed the work of Andraeson that both venae cavae can be clamped for 20 to 30 minutes provided the azygos venous flow continues, which means that no great quantity of blood need be provided by an external circulation to maintain life. In his technique the donor's (usually the mother) superficial femoral artery is cannulated and the blood passed through a small pump to the patient's aorta via the subclavian artery, the flow being reinforced when necessary from a reservoir of oxygenated blood collected from the arteries of other donors. The blood in

then returned from the patient's venae cavae by a second pump to the veins of the donor. After the establishment of the cross-circulation both of the patient's venae cavae are clamped and the heart is opened. Lillehei reported that, using this technique, 22 interventricular septal defects had been closed with seven deaths, two patients with the tetralogy of Fallot had been treated by closure of the interventricular septal defect and resection of the infundibular stenosis with one death, and in six patients the abnormality of atrioventricularis communis had been corrected with three deaths; there had been no donor mortality; the oldest patient of his series had been a 14-year-old girl weighing 100 lb. (45 kg.), but Lillehei felt that the method could be used with success in adults.

The discussion on the treatment of interatrial septal defects included the description of diagnostic aids by both ANDREW MORROW (Bethesda) and CLARENCE CRAFOORD (Stockholm). The former stated that with a small shunt the oxygen differences between the two sides of the heart might vary only slightly from normal, but that if nitrous oxide was used as a test gas the differences were greater. Crafoord described a double balloon catheter which could be passed through the septal defect: inflation of the balloons could then be used either to estimate the size of the defect or to block the defect and study the changes which this produced. Various methods of closure were described; both CRAFOORD and TYGE SONDERGAARD (Aarhus) used a strong non-absorbable ligature which they passed round the defect, guiding the needle with a finger placed in the atrium. CHARLES BAILEY (Philadelphia) showed how he had modified his patch operation, which he introduced in 1952, and also how it was possible to treat an associated mitral stenosis by passing a finger through the defect before its closure. And GILBERT BLOUNT (Denver) stated that Henry Swan, using hypothermia, had closed 24 secundum defects by a direct suture under vision. There had been only two deaths in this group, and all but two of the closures were considered to be complete when tested at the follow-up.

Patent Ductus and Transposition of the Great Vessels

Other aspects of congenital heart disease which were discussed included atypical patent ductus arteriosus. ROBERT ZIEGLER (Detroit) felt that a patent ductus entering below a coarctation (infantile ductus) should be operated on at an early age with closure of the ductus and resection of the coarctation. FRANK GERBODE (San Francisco) described 12 children with a balanced ductus (pressures the same on each side) treated by operation, all of which st.. have evidence of pulmonary hypertension, while one adult with the same lesion had done well; he also mentioned that he had diagnosed by pressure readings at operation one case of ductus with a reversed flow; this he had left alone. WILLIAM MUSTARD (Toronto) stated that transposition of the great vessels was the leading cause of death in congenital heart disease in infancy. There were three possible operations: transposition of the veins, cross-grafting of the great arteries, and transposition of the great arteries, including the left coronary. He preferred the last, and had performed it with the aid of an extracorporeal circulation using a monkey lung as an oxygenator on 16 infants, but had no success as yet. CRAFOORD and EARLE KAY (Cleveland) described their modifications of these procedures, but, like Mustard, their results had so far been unsatisfactory.

Diagnostic Techniques

Diagnostic techniques were discussed by many of the participants, including JOHN LIND (Stockholm), who described his technique of performing selective angiocardiography with a synchronous electrocardiogram, and BENGT JONSSON (Stockholm), who stressed the danger of repeated injections of contrast medium at the same session. RICHARD BING (Birmingham, U.S.A.), in an outstanding contribution, described some of his experiences with cardiac catheterization aided by a new type of catheter which could be bent in any direction by means of nylon threads to facilitate its passage through the heart. He had shown by coronary sinus catheterization that the relative contribution of carbohydrate and non-carbohydrate metabolism to the total myocardial oxygen consumption was in the range of only 24% for carbohydrate and 76% for non-carbohydrates such as fatty and amino-acids; and that in experimental coronary occlusion under hypothermia the metabolic effects of interruption of a coronary artery were much less severe than without hypothermia, probably owing to a reduction of enzyme activity.

REJANE HARVEY (New York) thought that it was logical to insist on the demonstration of raised pulmonary artery pressure by cardiac catheterization before advising mitral commissurotomy, in order to exclude those patients with myocardial insufficiency. OLGA HARING (Chicago) believed that in mitral stenosis of rheumatic origin there was always some regurgitation, and she used the electrokymogram of the left atrium to detect the degree of this regurgitation.

Mitral Valvular Disease

The treatment of mitral stenosis was discussed by a panel whose combined experience must have reached many thousands of operations. The main point which emerged was that technique and selection have now become standardized. On the other hand, the problem of mitral regurgitation, which was introduced by DWIGHT HARKEN (Boston), is still unsolved. He stated that the various baffle operations which he had introduced had proved unsatisfactory and that he was now trying to reduce the circumference of the annulus by open operation under hypothermia. ROBERT GLOVER (Philadelphia) was trying to do the same thing by inserting a purse-string suture around the valve, and four out of five cases had been improved by the operation. CHARLES BAILEY had now given up his pericardial flap operation and was using a piece of costal cartilage wrapped in pericardium in the hope of creating an adequate baffle. For aortic insufficiency he was passing a nylon suture around the valve ring in order to reduce its circumference.

Aortic Stenosis and Regurgitation

CHARLES BAILEY stated that he had performed 211 operations for aortic stenosis using the transventricular route, but that he now used a digital technique, the finger being inserted through a pouch of preserved homologous pericardium sewn to the aorta.

CHARLES HUFNAGEL (Washington) described his operation for aortic insufficiency using a leucite valve inserted into the upper descending aorta. He had operated on 80 patients with a hospital mortality of 20%. STANLEY SARNOFF (Bethesda) described the anaemia which usually develops during the first few weeks after this operation; it ceases spontaneously after this period, but has to be treated by transfusions of packed cells if relative coronary insufficiency and death were to be avoided.

Hypothermia

The panel on hypothermia which WILFRED BIGELOW (Toronto) conducted was divided into two groups: the majority, including DENTON COOLEY (Houston), HARRIS SHUMACKER (Indianapolis), and HENRY SWAN (Denver), favoured surface cooling, whilst Sir RUSSELL BROCK preferred veno-venous blood-stream cooling; all the participants favoured rapid rewarming. SWAN, in addition to the closure of atrial septal defects already mentioned, had used hypothermia on twelve patients with no deaths in whom he had operated on the pulmonary valve under direct vision. Another method of obtaining direct access to the heart was mentioned by CRAFOORD; using a complete extracorporeal circulation, he had resected a large myxoma of the auricle from a woman of 40, and she was alive and well one year later.

Aortic Aneurysms and Occlusive Disease

HENRY BAHNSON (Baltimore) reported that he had resected 26 aneurysms of the thoracic aorta, excluding coarctation aneurysms, with eight deaths, and COOLEY stated that he and MICHAEL DEBAKEY (Houston) had resected 101 abdominal aneurysms (17 of these had leaked prior to operation) with 18 deaths.

CHARLES ROB (London) gave the results of a follow-up of 93 homologous arterial transplants, the majority for occlusive arterial disease, inserted over a period of five years. He pointed out the good results which followed such surgery in the aorta, iliac, and some popliteal arteries, and the very careful selection which should be practised before a femoral transplant was inserted.

Blood Vessel Substitutes

This panel included ARTHUR BLAKEMORE (New York), who gave his views on plastic cloth. The most widely used material appeared to be orlon dipped in polyvinyl. ERIC NANSON (Saskatoon) was using nylon taffeta, which could be heat-sealed, thus making a seam unnecessary. In the field of homologous arterial transplantation OSCAR CREECH (Houston), HUFNAGEL, ROB, and EMERICK SZILAGYI (Detroit) used freeze-dried material. SZILAGYI had developed an outstanding method of sterilizing contaminated arteries with beta-propriolactone. CREECH and ROB were in agreement that the degree of ingrowth of recipient tissues was less than had been thought.

Just before the conclusion JAMES FRYFOGLE (Detroit) described a method of arterial suture using temporary split metal cuffs which may well revolutionize this branch of surgery. He stated that with this method he had transplanted the whole aortic arch of a dog in hypothermia time, with survival of the animal. It was a pity that time did not allow us to hear more from him.

Great credit is due to the organizers of this symposium, which was an outstanding success. The local members of the programme committee, Dr. ROBIN BUERKI, the executive director of the Henry Ford Hospital; Dr. CONRAD LAM, the symposium chairman; Dr. JOHN KEYES, the secretary; and Dr. EMERICK SZILAGYI and Dr. ROBERT ZIEGLER deserve the sincere thanks of all the participants. We understand that the proceedings of this symposium are to be published in book form by Saunders and Co. in about four months' time.

DOCTORS AND THE PRESS

An exploratory meeting between representatives of the Press organizations and the medical profession was held at B.M.A. House on March 29 (see *Journal*, March 12, p. 677) to discuss relations between the medical profession and the Press, particularly with reference to news from hospitals. Dr. H. Guy Dain (chairman of the Public Relations Committee of the B.M.A.) was in the chair, and the following attended:

Medical Representatives

Dr. E. A. Gregg, Chairman of Council, B.M.A.
Mr. L. Dougal Callander, Treasurer, B.M.A.
Dr. H. M. Cohen
Dr. F. Gray
Dr. D. F. Hutchinson
Mr. J. R. Nicholson-Lailey
Dr. A. Talbot Rogers
Dr. W. Woolley
} Members of Public Relations Committee, B.M.A.
Dr. Robert Forbes, Chairman of Central Ethical Committee, B.M.A.
Dr. J. G. M. Hamilton, Chairman of Journal Committee, B.M.A.
Sir Harold Boldero, Representative of Joint Consultants Committee.

Press Representatives

Sir Linton Andrews (General Council of the Press).
Mr. J. L. Palmer (Newspaper Society, also representing the Scottish Newspaper Proprietors' Association).
Mr. David Prosser (Guild of British Newspaper Editors).
Mr. Norman Robson (Newspaper Conference).
Mr. C. Webster (Scottish Daily Newspaper Society).
Mr. H. Gudenian (Periodical Proprietors' Association).
Mr. Edward Davies (Press Association).
Mr. Brian R. Roberts (Institute of Journalists).
Mr. H. J. Bradley (National Union of Journalists).
Mr. S. W. Rumsam (B.B.C., "Sound" Radio).
Mrs. Mary Adams (B.B.C., Television).

Mr. S. Heald represented the Ministry of Health as an observer. The Newspaper Proprietors' Association, which was to have sent an observer, was unavoidably prevented from doing so.

The meeting decided to establish a committee to examine the subject in detail and to formulate proposals for further consideration by the full meeting. The following were appointed to the committee:

Sir Linton Andrews	Dr. H. Guy Dain
Mr. H. J. Bradley	Sir Harold Boldero
Mr. H. Gudenian	Dr. R. Forbes
Mr. J. L. Palmer	Dr. F. Gray
Mr. David Prosser	Dr. J. G. M. Hamilton
Mr. Brian R. Roberts	Mr. J. R. Nicholson-Lailey
Mr. Norman Robson	Dr. A. Talbot Rogers
	Dr. W. Woolley

It was decided to invite the Newspaper Proprietors' Association to nominate a representative to the committee. The first meeting of the committee will be held on Wednesday, April 27.

Nova et Vetera

MEDICAL ART AND HISTORY IN EXETER

Under the auspices of the Devon and Exeter Medico-Chirurgical Society a medical historical exhibition was opened on March 31 by Dr. J. W. Cook, F.R.S., Principal of the University College of the South-West. The exhibition is centred on the classics of medical literature from the library of the Cathedral Church of St. Peter, Exeter, and from the Exeter Medical Library; it also includes documents from the city archives relating to the ancient Exeter hospitals, and documents and portraits from the early years of the Royal Devon and Exeter Hospital. Thus it provides an introduction to medical history of interest alike to lay as well as to medical men and women. But more than this is attempted, and the exhibition gives emphasis to the beauties of sixteenth-century printing in Italy and the excellence of engraving up to the end of the eighteenth century.

Although to modern thought the idea of a provincial metropolis may be contradictory, it was quite otherwise up to the end of the eighteenth century. Then the city played a dominant part in the life of the south-west of England. It was the focal point of religious and social affairs, of government, industry, and commerce, and it provided leaders in medicine. In the early nineteenth century it had its own medical school. The Church has played an important part in medical history, as is to be seen from the possession by Exeter Cathedral of many of the more important classics of medical literature up to the early part of the eighteenth century. These include a fourteenth-century manuscript copy of John of Gaddesden's *Rosa Anglica* and an incunabulum of Celsus. Hippocrates, Galen, Manardus, John of Vigo, Vesalius, Eustachius, Paré, Fabricius, Spigelius, Harvey, Sydenham, and many others are represented. In the Exeter Medical Library the seventeenth, eighteenth, and early nineteenth century are particularly well covered. A very special attraction is the Vesalius *de Fabrica*, represented by a handsome copy of the great 1555 edition, the 400th anniversary of which is commemorated in the illustrated catalogue available. Among the City of Exeter's archives are documents relating to the foundation of the first hospital in the city, that of St. Mary

Magdalene in the twelfth century. It was first devoted to lepers, then to the scrofulous, and to-day, on a new site, is an almshouse. In addition the exhibition is showing a large Hunter collection, which also touches upon the work of the Hunterian disciples, including the eccentric genius John Sheldon, who worked for the last twenty years of his life in Exeter.

The Royal Devon and Exeter Hospital, many of whose portraits and early documents are on view, was founded in 1741 during the social revolution which saw the beginnings of several other notable provincial hospitals as well as most of the London teaching hospitals of to-day, apart from Bart's and St. Thomas's.

The exhibition has been organized by the president of the Devon and Exeter Medico-Chirurgical Society, Mr. Norman Capener, and is open throughout the month of April from 1.30 to 5.30 p.m. daily.

Reports of Societies

LOCAL MEDICAL SOCIETIES

Liverpool Medical Institution

The value of "C-reactive protein" as a sensitive test for activity in rheumatic fever and tuberculosis was discussed in a contribution to the Institution on March 24 by Dr. S. E. KEIDAN, lecturer in child health at Liverpool. In 1930, he said, during investigations of the chemical and immunological properties of pneumococci, Tillet and Francis had isolated a polysaccharide (Fraction C) from the bacterial body which was found to form a precipitate with the serum of patients suffering from various infective illnesses. Precipitation occurred only during the acute phase of the illness and could no longer be demonstrated after recovery. In 1943 Löfstrom independently reported the occurrence in human serum of a substance which caused capsular swelling and agglutination of pneumococci. The substance was found only in the serum of patients in the acute stages of various bacterial diseases or with conditions characterized by tissue destruction. It was later suggested that this substance was identical with the precipitin for C-polysaccharide which had been previously described. This precipitin, C-reactive protein, was eventually separated from serum and obtained in crystalline form. It proved highly antigenic to rabbits, and the antiserum produced is a sensitive test for its presence in serum.

Clinical studies in rheumatic fever, continued Dr. Keidan, had shown that the detection of C-reactive protein in the serum is both the most consistently positive laboratory index of rheumatic activity and the most sensitive. The test is, however, non-specific, and may be positive in myocardial infarction and malignant disease as well as in the presence of any inflammatory process. His own studies, using rabbit antiserum, had been done on 70 children with a variety of illnesses. In 16 cases of rheumatic fever, 11 with polyarthritis gave positive tests, 2 cases with chorea and carditis gave positive tests, and 3 cases of pure chorea gave one negative, later becoming positive, and 2 weak positive. Four suspected cases gave negative results in 3 cases and positive in the other; none of them developed further evidence of the disease. One child in congestive failure had a very low sedimentation rate but a strongly positive test for C-reactive protein. Fifteen cases of tuberculosis were studied. Five out of six patients with primary infections gave positive tests, and in the one who was negative there was doubt about the activity of the disease. Two cases of meningeal and two of miliary tuberculosis were positive. Two cases of pleural effusion were negative, one later becoming weakly positive. Of two cases of post-primary disease, one was negative and one positive. Tests in children suffering from other infections were usually positive. In 32 newborn babies, 28 gave negative tests, and the four who were positive were found to be unwell, either with infection or with a history of anoxia at birth.

It was suggested that C-reactive protein might be an antibody precursor, and that its persistence in rheumatic fever might be due to an inherited or acquired failure to synthesize a particular type of antibody against haemolytic streptococcal infection.

Manchester Medical Society

Twenty-three babies out of every 10,000 born alive require general surgical operations in the first month of life, according to figures given by Mr. A. JOLLEYS, a Manchester paediatric surgeon, in a contribution to the Section of Surgery on March 8. Most of the congenital malformations from which these babies suffer are remediable. In intestinal and oesophageal surgery both practical experience and the results of experimental work suggested the value of simple end-to-end anastomosis with one layer of unabsorbable sutures. The early diagnosis of many of these malformations was of paramount importance, and it was essential to carry out a routine examination of the child at birth.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

The Ban on Heroin

SIR,—Your annotation (*Journal*, July 25, 1953, p. 196) on the omission of heroin from the *British Pharmacopoeia* suggested that this should be a precedent for Government authorities to make the use of the drug illegal. I protested in a subsequent letter (*Journal*, August 8, 1953, p. 338) to you, but my voice was of one crying in the wilderness. With sinister failure to seek the views of the profession as a whole, the Government has now decided to implement the recommendation of the Economic and Social Council of the United Nations regarding the manufacture and use of heroin. After the expiry of the current licences for the general manufacture and import of heroin under the Dangerous Drugs Act, small quantities will be manufactured in this country for scientific purposes only and the import of the drug will not be permitted. The full implication of this astonishing move is certainly not grasped by the majority of practitioners. It is nothing more or less than direct interference with our liberty to prescribe for patients what we think is best for them.

The ban on heroin is being imposed not in response to any demand for such action in Great Britain, but solely as the result of political pressure from foreign countries, notably the U.S.A. and the World Health Organization. The United States has a vast problem of drug addiction, and has since 1925 forbidden the manufacture or importation of heroin. The result could have been foreseen. Addiction is still rife there because the cost of the drug has rocketed. This provides the stimulus for the black marketeer to take any risk to spread the heroin habit. The lessons of prohibition and opium control have been as seed fallen on stony ground.

Pain, the most clamant of all symptoms, must be relieved. Have our legislators been advised that morphine causes severe vomiting in 10% of patients, or that pethidine, a drug of addiction, is less reliable than heroin, and is also frequently emetic in action? Have the medical advisers, who are presumably behind this move, forgotten that codeine, except in constipating and highly depressant doses, may not ameliorate the cough of tracheitis? The fact is there is no complete substitute for heroin. Our D.D.A. is a highly effective agent to discourage addiction. This governmental ban will inflict untold hardship on a multitude of patients in a futile attempt to save foreign decadents from addiction.

Clinical practice must be kept free from political interference. The views of the royal colleges and general practitioners should always be sought on matters of this kind. Let us not view meekly the sacrifice of freedom on the altar of woolly humanism.—I am, etc.,

London, W.1. A. H. DOUTHWAITE.

Chicken-pox Quarantine

SIR,—Dr. M. Curwen (*Journal*, March 19, p. 727) asks the pertinent question: "Is it really necessary to exclude children with chicken-pox from school?" Certainly, in junior schools, it could be argued that it would be more logical to take steps to spread chicken-pox rather than attempt to control it. Chicken-pox is such a prevalent disease that few, if any, of us can hope to escape exposure to infection during life. Whereas an attack experienced during early school life is likely to be mild and to occur at a time of least inconvenience, an attack later in life tends to be more severe and to occur at an inopportune moment, interfering with important events such as examinations and big sporting occasions, a good topical example being this year's Cambridge boat race crew.

I think that Dr. Curwen is right in suggesting that very many children are excluded from school for an unnecessarily long period on account of this relatively trivial disease. There is very little, if any, evidence that cases of chicken-pox remain infectious for longer than five or six days after the appearance of the rash. During this period most patients are suffering clinically from the disease and are better resting at home, even if not in bed. At the end of a week, however, if the clinical condition permits, I see no reason why patients should not return to work and children to school. The present policy of waiting until each and every scab has separated before release from isolation is far too rigid, and, as Dr. Curwen has indicated, gives rise to a lot of unnecessary absence from school and to parental frustration. In special circumstances, such as the admission of a case to a paediatric unit, it may be advisable to play for absolute safety and wait until every scab has separated, but the vast majority of cases could be released from isolation much sooner, and a period of one week from the appearance of the rash would, in my view, be quite adequate.—I am, etc.,

Oxford. J. F. WARIN.

SIR,—Dr. M. Curwen (*Journal*, March 19, p. 727) recommends the ignoring of all precautionary treatment in an attack of chicken-pox. I venture to suggest that there is one very important and sometimes dangerous complication, the onset of which would be made all the easier by such procedure—namely, acute nephritis. One of the worst cases I ever saw of this disease was during the later stages of an attack of chicken-pox in a child whose parents had either overlooked or had ignored the attack and had allowed the child to lead a normal life.—I am, etc.,

Southsea. M. ASTON KEY.

Natural Childbirth

SIR,—My letter on the subject of natural childbirth (*Journal*, February 19, p. 475) was deliberately provocative; I set out to try to rock the boat. Unfortunately prejudice and immature reasoning have tended to distort the argument. May I therefore clarify some points? (1) I did not condemn preparation for childbearing, only "special training"; of course we all prepare our mothers in one way or another. It is over-elaboration in teaching and training that I see as a danger. Even Dr. Anthony Ryle (*Journal*, March 19, p. 725) admits that there may be a case for simplifying and shortening. (2) My main attack was on training for the second stage of labour. All my experience and reasoning rebel against this practice. On the question of the first stage and relaxation exercises I left an open verdict. (3) I do not disapprove the quest for painless childbirth—quite the reverse. I am afraid Dr. Ryle, and possibly others, misunderstood the phrase where I was praising the pioneer work (thinking particularly of Dr. Grantly Dick Read) which weaned women away from demanding painless labour by artificial means. Twilight sleep, unnecessary forceps delivery, and even caesarean section were demanded by some women not so very long ago to save them from pain in labour. (4) The extravagance to which I was alluding was the tendency for local authorities and other bodies to appoint special personnel, often without full midwifery knowledge, to run clinics to train women for childbirth. I believe that all teaching should be given by the doctor, midwife, or hospital team who are going to look after the same woman in labour. Is Dr. Ryle putting the clock back or using false considerations of economy when he teaches his patients himself? (5) There is a danger that, either from inexperience or from too great enthusiasm for one particular facet, we lose sight of the fact that with modern improvements in labour management, even without all the palaver beforehand, women on the whole are having satisfactory confinements. Patients have recently been heard to say that books and classes make it all seem so much more complicated than it really is. (6) In a process with such a high rate of normality we must assess our results by focusing attention not on the successful cases but on the failures. Unfortunately the less successful tend to keep quiet, overshadowed by a feeling of frustration and inadequacy, while the successful ones are only too ready to applaud, particularly when it has been instilled in them that their own skill has played so large a part. Would that more Mrs. Constance Lynns (*Journal*, April 2, p. 851) came forward and that the Mrs. Honor Kennys (*Journal*, March 26, p. 785) would reason out that it is no praise of any method if it takes a previous confinement and a physiotherapist standing over them to achieve a satisfactory second birth. (7) My plea is that the way should be left open to allow of trial of a variety of methods and that we should not be too ready to accept or to publicize that any particular regime is right in its entirety. Knowledge of childbirth, like knowledge about sex, should be instilled gradually during the process of growing up. Only "topping up" would then be required when the time came.

It seems by implication that my experience to form an opinion on this problem has been doubted. To Dr. Grantly Dick Read (*Journal*, March 5, p. 604) I would say that I base my views on 18 years of private obstetric practice with complete and personal care of some 900 women, the majority of whom achieved normal birth, as well as on my observation in consultant practice. To Mrs. Kenny I would say that I, too, am a mother (of four), but I believe that personal experience should not be given undue weight. From the midwife's point of view I can only speak through having been very closely associated with them for many years. It is certainly not my finding that their instructions to women in labour are of little or no avail. With experience they give very few, because they learn that nature directs the process better than they can if allowed to do so.

Finally, I will not accept Dr. Ryle's suggestion that "civilized social beings" are beyond hope of natural childbirth. Some, it seems, would nearly go so far as to imply that women require psychiatric treatment before being able to achieve their natural heritage of bearing children. Please let us keep our sense of proportion and help women to take childbearing in their stride, regarding it as a normal, natural, and not unduly difficult process.—I am, etc.,

Hove. CONSTANCE L. BEYNON.

Environmental Factors in Cervical Cancer

SIR,—Dr. Ernest L. Wynder's paper (*Journal*, March 26, p. 743) made very interesting reading. In particular, I would commend his statement that international co-operation is of importance in achieving "more conclusive results than can be obtained from any one country alone." Among U.S.A. Negroes he found the rate of cervical cancer "high," the age of first coitus "early," and circumcision state and penile hygiene "poor." May I suggest that this important

research be extended elsewhere? For example, figures from Nigeria, where the Ibos—of pure Negro stock—have a 100% male circumcision rate, may go further to elucidate the place of epidemiology in the investigation of cervical carcinoma.—I am, etc.,

Glasgow, C.3. W. I. B. ONUIGBO.

Hypodermic Injection Technique

SIR,—Dr. L. P. Lockhart (*Journal*, February 12, p. 415) rightly calls attention to the danger of injections being given without first withdrawing the plunger of the syringe. But, passing from the dangers to the discomfort of injections, may I mention a simple way of reducing the pain caused by injections? Needless to say, the smaller and sharper the needle the less the pain, but a satisfactory needle is only one of the secrets of semi-painless injections; the other and more important is this.

When about to give the injection let the needle of the loaded syringe rest lightly on the skin so that the patient, although conscious of its touch, is unaware of its sharpness; *continue to hold it thus for five to ten seconds*, and then suddenly, and as quickly as possible, pierce the skin to the necessary depth. With this technique many babies being immunized against diphtheria neither cry nor register pain, and many adults with previous experience of receiving injections have remarked, "That was the most painless injection I have ever had."

I think the explanation for the relative freedom from pain when injections are given in this way is that the stimuli of touch and pain are thereby separated. It was Pavlov, I believe, who stated that the brain cannot react to more than one stimulus at one time. A slap may cause one to jump, and momentarily one is uncertain whether the slap was a painful or painless touch. When, however, the touch is accompanied by pain (as in the case of an injection) the perception of pain seems to dominate that of touch, and the stimuli of pain and touch are both recorded by the brain as pain. The pain therefore becomes magnified. On the other hand, when a stationary object has been gently touching the skin for a period, one ceases to be conscious of it—for example, as in the case of the clothes one wears. By dissociating touch from pain and adopting the simple technique mentioned, scores of thousands of injections every day could be made relatively painless.—I am, etc.,

Reading. K. D. SALZMANN.

Dermatomyositis

SIR,—The case described by Dr. Hillas G. Smith (*Journal*, March 26, p. 770) does not appear to me to be that of dermatomyositis. The diagnosis seems to have been made on the increased creatine output in the urine, together with "skin and muscle involvement."

The skin and muscle involvement appears to be that of painful erythema and swelling over painful joints and muscles, following a history of severe tonsillitis. Acute dermatomyositis usually starts as an acute febrile illness resembling influenza, with shivering attacks, hyperpyrexia, and general muscle aching, but no joint involvements. The face is involved first, with erythema and swelling—the infra-orbital swelling being marked and persistent. The patches of erythema are diffuse and not confined to joint areas. The patient complains that he cannot carry out certain movements, not because his joints are painful but that he just cannot do it—i.e., his muscle power is lost.—I am, etc.,

Bradford. ALLAN BIGHAM.

Grants for New Hospitals

SIR,—Dr. J. M. Alston (*Journal*, March 26, p. 789) has misread my letter (*Journal*, March 5, p. 600) on the subject of grants for new hospitals. I did not advocate the patching up of old hospitals (indeed, I have worked for too long in such places), nor did I object to the building of new hospitals. I cited specific examples of a situation in the North-west Metropolitan Region, where I advocated new buildings for some of the old hospitals in addition to, or even instead of, some of the proposed new hospitals. I am, of course, well aware of the fact that, even with the latest proposals from the Ministry, we shall be doing only a fraction of the hospital building which was taking place immediately prior to the war. This being so, it is surely all the more important to re-examine the present building programme, and to ensure that the needs of the public will be properly and economically satisfied. In many instances it will prove much easier to rebuild old hospitals (in part or in whole) rather than to build new ones and then be faced with additional staffing problems and overhead expenses.

I stated in my last letter that local medical opinion had not so far been consulted. I have since been informed that the Management Committee in the area concerned has also not been consulted. This is surely a curious and deplorable state of affairs, and I feel certain Dr. Alston will agree that the gentleman from Savile Row does not always know best.—I am, etc.,

Radlett, Herts. R. S. MURLEY.

Post-maturity and Asphyxia

SIR,—Dr. E. Robert Rees (*Journal*, March 19, p. 723) draws attention to a danger which is, I am sure, not generally recognized among midwives, or perhaps even among some doctors. I refer to the fact that in some cases of post-maturity the placenta has diminished in efficiency and the oxygen supply to the foetus is only just enough to maintain its life. The placental circulation is interrupted during a prolonged second stage contraction and asphyxia may well result. How often has one seen or read of large, healthy-looking post-mature boys born after a prolonged labour but unfortunately dead on arrival. The nurse's satisfaction at having maintained an intact peritoneum is a very poor compensation for this misfortune.

One remedy is of course an episiotomy done without delay, and followed by forceps if necessary. I should also like to stress that the use of gas-and-air analgesia may very well be enough to turn the scale against the child's survival. The medical certificate of fitness for gas and air refers only to the mother, and is given at a time when post-maturity has not entered the picture. I do not know whether this is pointed out to midwives in their gas-and-air training, but very much doubt it. I also think that local authorities issuing these sets should consider the fact that in certain circumstances they are potentially lethal weapons.—I am, etc.,

Shipley. HENRY S. RUSSELL.

Post-puerperal Recurrent Depression

SIR,—I have read with interest Dr. A. B. Hegarty's paper on post-puerperal recurrent depression (*Journal*, March 12, p. 637). Any paper which draws attention to the fact that premenstrual symptoms are common, often severe, rarely treated, and usually curable is to be welcomed. But I fail to see in what respect the condition he mentions differs from the premenstrual syndrome which has so often been described, most fully by Dr. Dalton and myself.[1] He quotes previous mention by Hemphill and by Rees, but dismisses their statements as "the passing remarks of writers who were dealing with a different theme." The rest of the extensive "literature" is left out altogether, except for a brief mention of the work of Stieglitz and Kimble and of Bickers and Woods.

Why "a different theme"? It would appear that the right of Dr. Hegarty's syndrome to a separate existence rests upon his selection of patients who, in addition to the main complaint of ovulatory or premenstrual mental disturbance, have a pyknic build, have suffered from puerperal depression, and have irregular menses. On this principle medical literature would soon be overburdened with syndromes. If one looked for them one could probably collect a number of cases of a most interesting and hitherto undescribed condition of acute appendicitis occurring in blonde women with ingrowing toe-nails whose husbands are heavy smokers (will Dr. Horace Joules please note?).

I do not propose to examine again the case records of the 84 patients described by Dr. Dalton and myself, but I feel quite sure that many of them were pyknic, many of them had irregular menses, and some of them had had puerperal depression. Many of them had flat feet, too.—I am, etc.,

London, W.1. RAYMOND GREENE.

REFERENCE

[1] Greene, R., and Dalton, K., *British Medical Journal*, 1953, **1**, 1007.

Adrenocortical Activity and Puerperal Depressive States

SIR,—In his enlightening article (*Journal*, February 26, p. 495) Dr. R. I. S. Bayliss has revealed some interesting data on the blood levels of 17-hydroxycorticosteroids during pregnancy and the puerperium. It appears that the high mean level of 24 μg. per 100 ml. blood occurring during the last month of pregnancy falls rapidly after parturition, reaching a normal value by the eighth post-partum day.

It is now well known that the sense of well-being and elation experienced by many patients receiving A.C.T.H. is liable to give place to a temporary depressive phase when the drug is withdrawn. It might be, therefore, that the mental depression so common in women during the second week of the puerperium is associated with the relatively sudden fall in circulating corticosteroids which Dr. Bayliss describes. If this is so, then the more severe case of puerperal depression, showing obvious deterioration, might be tided over this critical period by the administration of gradually diminishing doses of A.C.T.H.—I am, etc.,

Leeds, 2. K. A. EXLEY.

Manipulation and Low Back Pain

SIR,—Drs. Anthony B. Coyer and Ian H. M. Curwen (*Journal*, March 19, p. 705) have compared the treatment of low back pain by manipulation with treatment by bed rest and simple analgesics. In assessing their results they have analysed all the 76 patients treated by manipulation, but only 60 of the 76 patients who were advised to go to bed and take simple analgesics. The reason for the exclusion of these 16 patients is that they "did not carry out instructions or did not report for assessment." No information is given about the results in these 16 patients, and if it is assumed that all of them did well the apparent differences between the two treatment groups will largely disappear. It is a great pity that no information is provided about the discarded 16 patients, since their exclusion destroys the value of what would otherwise have been an interesting study.—I am, etc.,

Manchester. J. H. KELLGREN.

Pre-employment Examinations

SIR,—The Chief Inspector of Factories in his Annual Report for 1953 refers to the fact that the number of first examinations for employment under the Factories Act (269,379) was larger than the number of subsequent examinations (218,367), whereas the reverse would be expected. A probable explanation lies in the fact that several "first" examinations are done in respect of some young persons, as, if they move from the area of one A.F.D. to that of another, form 71 (card for the use of A.F.D.) does not follow them. Indeed, it may happen that it does not follow from job to job even within the area of one A.F.D., since a new card is prepared by the employer for the first examination at the place of the new employment. The A.F.D. will use this, and if he files the cards by factories the duplication will not come to light.

The reasons for refusal of certificates of fitness, which the Chief Inspector lists in table L1 of his report, may not present an accurate picture of the health of young persons seeking factory employment, since many applicants are seen by a works medical officer before being taken on. Thus the A.F.D. to a factory which has its own medical officer is likely to have a very small number of rejections. Where the works doctors is also the A.F.D. the number will be nil. Of course, an unsuccessful applicant can always try his luck elsewhere, and if he is again unlucky his particular defect will be twice recorded.—I am, etc.,

Wraxall, near Bristol. ROGER WEST.

REFERENCE

[1] Cmd. 9330. H.M. Stationery Office, London.

Clinical Board Meetings

SIR,—I have recently returned from 14 months in North America, most of which was spent in one fairly typical city hospital in the U.S.A. There was one particular feature which does not seem to be generally known here and which I think should be widely adopted in the hospitals in this country. I refer to the so-called board meetings which are a regular feature in nearly all American hospitals. The commoner boards are the tumour boards, the pathological boards, the endocrine boards, etc. The great benefit of these boards might be clarified if I were to mention how one example, the tumour board, worked.

To its weekly meeting came physicians, surgeons, gynaecologists, pathologists, the radiotherapist, the radiologist, and any other interested consultants, as well as the housemen. Interesting and perplexing tumour cases were presented. Someone familiar with the case, usually the consultant or his houseman, would give the relevant history, physical findings, and results of investigations. The patient would then be examined by those at the meeting. A discussion would follow, directed by the chairman of the board, on the diagnosis, treatment, and prognosis of the case. A healthy sign was the frequency of open disagreement and the sympathetic attention paid to the opinion of the lowliest houseman. The board would finally advise the course of treatment, but the consultant whose case it was was in no way obliged to follow the recommendation of the board, though he nearly always did so. The end of the meeting was devoted to follow-up cases previously presented, with reports of progress.

I feel that the institution of boards of this nature would be of material benefit to British doctors and to the patients they aim to serve.—I am, etc.,

London, N.18. MICHAEL C. LATHAM.

Anticholinergic Drugs for Peptic Ulcer

SIR,—The final paragraph of the leading article (*Journal*, March 19, p. 711) calls for comment. Is not the appreciation of "brand-new treatments" by patients often short-lived? The "brand-new" description will often convey to them a major advance in therapy, leading to high hopes and ultimate disillusionment. It may give patients the impression that the doctor is doing his best for them, and help to satisfy the emotional dependence which the chronically ill are apt to develop with regard to their doctor. But surely we should encourage as many as possible to develop a courageous understanding of their ailment, and discourage the hypochondriasis which so frequently results from over-treatment. We should also remember we are doctors, not salesmen, whether public money is involved or not.—I am, etc.,

Barton-on-Humber, Lincs. S. H. F. HOWARD.

Bolus Obstruction

SIR,—Having read reports of small bowel obstruction resulting from the impaction of a variety of undigested foodstuffs (*Journal*, December 18, 1954, p. 1484, and November 27, 1954, p. 1301) we would like to record our recent experience in the management of a patient with small-bowel ileus where the impacting bolus consisted of undigested meat.

Recently a female of 67 years was admitted to Hammersmith Hospital complaining of central abdominal pain and vomiting of eleven hours' duration. The onset was abrupt, and the vomiting was associated with bouts of colicky pain. Clinical examination revealed an elderly edentulous patient having obvious attacks of intestinal colic accompanied by vomiting and with a soft non-tender abdomen. No mass was palpable and no evidence

of the cause of the obstruction could be found. It was decided to observe her overnight, during which time a piece of undigested meat 3 cm. by 2 cm. by 1 cm. was discovered in the vomit. Further questioning revealed that 12 hours prior to the onset of symptoms the patient had eaten a meal of sheep's heart and sausages which she had not masticated properly because of ill-fitting dentures. A tentative diagnosis of bolus obstruction was made, and, as the clinical signs of unrelieved obstruction persisted, laparotomy was performed. This revealed a firm rubbery bolus impacted in the terminal ileum about 90 cm. from the ileo-caecal valve. The ileum above this point was dilated and congested. The mass was with difficulty milked into the caecum and the patient made an uneventful recovery. Small pieces of meat but no bolus were recovered from the stools post-operatively.

In a review of 178 cases of bolus obstruction, Ward-McQuaid[1] found no case of obstruction from this cause. But from our experience in this case it is clear that to the long list of possible ingredients of an impacting food bolus we must now add incompletely masticated meat.

We are grateful to Mr. M. R. Ewing, F.R.C.S., for advice and permission to record this case.—We are, etc.,

G. E. ALLIN.
J. G. BRICE.

London, W.12.

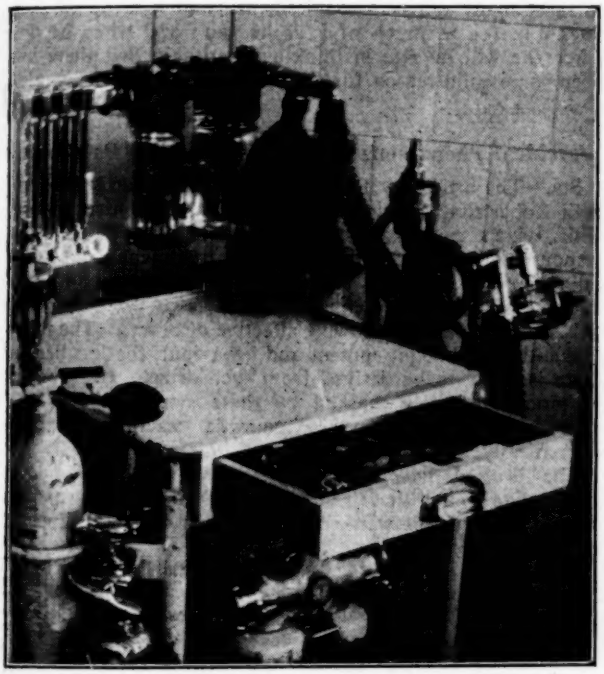
REFERENCE

[1] *British Medical Journal*, 1950, 1, 1106.

Additional Drawer for the Boyle's Machine

SIR,—I find that at the start of an operating session the essential anaesthetic accessories—laryngoscope, Magill's forceps, mouth gag, etc.—are neatly laid out on the top shelf of the anaesthetic machine, but in a short time the maintenance of this state of neatness, however desirable, becomes something of a nuisance.

In an attempt to obviate this difficulty I designed the drawer unit illustrated for the B.O.C. Boyle's apparatus. This unit fulfils two important criteria: (1) An unobstructed top shelf is provided. (2) There is adequate additional storage space for the essential anaesthetic accessories just at the anaesthetist's hand.



The unit, which was made by Mr. Young, of the Belfast City Hospital Works Department, consists of a wooden box-like structure which has a washable plastic top, and contains a drawer of the greatest possible size—that is, 15¼ × 13 × 2 in. (40 × 32.6 × 5.1 cm.). It is fitted in place of the original glass top shelf of the Boyle's apparatus and occupies the space between the upper structural frame and the under surface of the surrounding guard rail. This latter forms a lip around the edge of the new top shelf. In use the drawer has been found to be large enough to hold the laryngoscope, mouth gag, Magill's forceps, airways, connectors, lubricating jelly, cylinder key, etc., and has been proved to be of great practical value.

I wish to thank Dr. James Sutcliffe and Mr. J. Poots for the photograph.—I am, etc.,

Newtownards, N. Ireland. J. A. MCNEILLY.

Fluoridation of Public Water Supplies

SIR,—In their letter (*Journal*, March 26, p. 789) Drs. H. M. Sinclair and Dagmar Wilson, in a kind reference to me, mention a visit I made to an Oxfordshire village at Dr. Wilson's invitation to see and verify some of her cases of fluorotic teeth in the early days of her investigation.

Dr. Wilson has done an immense amount of work on this subject and I have done nothing since 1933, for lack of the necessary laboratory experience. I feel, therefore, some reluctance to offer criticism. I did, however, have the advantage at that time of having been able to examine in detail the teeth of a whole series of Maldon school-children, including all the age groups up to 16, and the further advantage of familiarity, as a dentist, with teeth in general, and I am sure that Dr. Wilson will not mind my correcting her implication that I verified all her findings. There was, among the fairly mild cases of fluorotic teeth, one apparently marked one showing dense brown staining which on closer examination we discarded because the stain proved to be superficial and could be removed, though with difficulty.

This incident is only of significance in connexion with the possibility mentioned by others that occasional cases can occur closely resembling mottling whose aetiology is in doubt. I have recently been shown another such case by Mr. Howell, of the Royal Dental Hospital; this was a variety of congenital amelogenesis imperfecta, and the stain was not removable.—I am, etc.,

London, W.1. N. J. AINSWORTH.

SIR,—My interest in this subject has recently been aroused not only by the correspondence in the *Journal*, but also by being asked by a patient, who apparently resides in one of the proposed "experimental areas," whether an increase in her fluoride intake would be injurious to her health. So far the evidence as to whether there is any risk of physical disease by adding 1 p.p.m. of fluoride to the water supply is most controversial. No mention, however, has been made of the possible psychological effect on a nervous patient who is forced by a medical officer not known to her, or by a committee of laymen, to increase her consumption of fluorides.

Surely some method of ensuring an adequate intake of fluoride in children up to the age of 14 years could be devised and the general practitioner allowed to advise his patients, to the best of his judgment and ability, about the taking of this potentially lethal substance.—I am, etc.,

Bangor. EYNON VAUGHAN.

Hydrocortisone Ointment in the Eczemas

SIR,—I was extremely interested to read in Dr. R. Church's paper (*Journal*, February 26, p. 517) and your annotation (p. 530) on the use of topical hydrocortisone in various dermatoses confirmation of my own limited experience with this type of therapy. It would seem evident that sufficient trials have now been carried out to evaluate the worth of this new therapeutic agent, and to establish that there are no dangers attached to its use.

Skin conditions, I find, make up a large proportion of one's general practice, and many of these prove quite intractable to the treatments readily available to G.P.s. Consequently, with the long-term and diverse treatments one has recourse to, these cases may tend to cost the N.H.S. large but "hidden" sums. One imagines that the only reason hydrocortisone ointment is not freely available is one of cost; but if this new agent will control symptoms, and

perhaps cure much more quickly, then surely it will prove to be more economical, if not cheaper, on a weight-for-weight basis than tar and zinc ointments. When can we in general practice hope to be free to prescribe this valuable addition to our pharmacopoeia ?—I am, etc.,

Manchester. S. EDEN.

Treatment of Pulmonary Tuberculosis

SIR,—Regarding any tuberculous infection and its effects, there are, since Koch's epoch-making discovery in 1882, many well-known factors. Of these, weight of infection, site, virulence of the organism, natural resistance of the host, allergy, and acquired immunity are the time-honoured "big five." Time was when the relative significance of these factors, *inter se*, largely dominated the whole clinical course of a tuberculous patient's illness. By and large good general health and greater natural resistance went hand in hand, so that the poorer-class patient had a greater chance of dying—but even here there were exceptions, particularly where the soil was virgin. There is much evidence that mortality and morbidity from tuberculosis are declining, but it is at once clear that, depending only on better social standards and the like, it would be a long time indeed before the disease became epidemiologically insignificant.

Fortunately, the "big five" above mentioned are no longer supremely important. Though one would be hesitant to say they now merely jutted up as rocks in a sea of new discoveries, nevertheless the old horizon has been shattered. Following hard on the discovery and development of antibiosis and chemotherapy and the ever-rising standards of anaesthesia came the increasing significance of thoracic surgery in tuberculosis. As the old horizon fell away, new vistas hitherto undreamed of—unless by the prescient—were opened up. And it is now not hard to understand why the patient's attitude to tuberculosis is being transformed. The *mens sana* is being established.

I cannot, in any degree, bear out Dr. J. F. Brailsford's sanguine remarks (*Journal*, March 12, p. 665) regarding current trends in the treatment of pulmonary tuberculosis. "Pleasant" is hardly a suitable adjective for any surgical operation—despite the advances in anaesthesia—and mutilating, in a sense, it can be. But pleasant it is indeed to find that those of our patients who have been transferred for surgical treatment return to continue their convalescence renewed not only in body but obviously in mind also. Here it is apposite to make a few additional observations. In the majority of our cases major operation has been performed under infiltration analgesia, yet terror, anguish, and psychological upheaval are absent. Most of these patients return —some quite soon—to self-supporting employment. The recurrence of positive sputum is rare. Hospitalization has been considerably reduced—especially now, as waiting-lists shrink. Further, the grossly swollen waiting-lists until recent times surely bear witness to the inadequacies of the past. Treatment may have been "most pleasant and enjoyable," but, despite any amount of honest endeavour, it had gross limitations. In assessing any method the results are all-important.

It is surely timely now to express the hope that when the reservoir of chronic infection has been effectively drained by the thoracic surgeon, and those unfortunates who developed their disease too early to be redeemed by chemotherapy, etc., are no more, then the family doctor with the facilities which are at his disposal will ensure that tuberculosis never gets beyond the earlier stages at which, in modern times, it can be adequately dealt with in the home.—I am, etc.,

Stornoway. EWEN A. CAMERON.

The National Formulary, 1955

SIR,—Dr. T. W. G. Kinnear (*Journal*, March 19, p. 725) can hardly expect his criticism of my letter (*Journal*, February 26, p. 541) on the *National Formulary* to be taken as anything but a leg-pull, but, seeing you have published it, may I reiterate that, though we all wish prescribing to be sensible and honest, the use of these adjectives in your leading article (*Journal*, February 12, p. 402) did imply that those who disagreed with the writer were not sensible or honest—which is, I think, untrue and certainly regrettable. If Dr. Kinnear had read your leading article he should have noticed that you used the term "ammonia and senega mixture" which I repeated, and which, incidentally, was more correct for my purpose, for many variants of this mixture have been used throughout the years.

I am sorry Dr. Kinnear cannot see my point about tablets, but although the new *National Formulary* does in one case prescribe a quarter of a tablet to be used—against which I protested, as one cannot expect many mothers to divide a tablet into reasonably equal quarters—the variations in dosage from infancy to adult life can seldom be properly graded with tablets, whereas they can with mixtures : and the variations between thirds, quarters, fifths, etc., of a tablet are much greater than those of the household teaspoon, etc. The point of mentioning economy was that it is, unfortunately, not uncommon to order 100 tablets and patients can easily carry them—and often leave many unused—but few doctors would order the equivalent 40 oz. or Winchester quarts for their patients to take away.

Similarly about "overburdening" the prescriber. In a mixture there are rightly main ingredients and adjuvants or modifiers. To get the same effect—which is a correct therapeutic aim—one would have to order a number of tablets or remember the name of the innumerable combinations which are quite justifiably being offered. It is no secret that the pundits condemn these, as Professor Dunlop did the comparatively simple "drinamyl" at Glasgow last year ; though, to my knowledge, if the question had been handed to one of the other members of the panel he would have said it was a most valuable tablet. When we get this acute difference of opinion between the academic and the G.P. or even the consultant, it is inevitable that opinions on the content as well as the format of the *Formulary* should also differ widely. Few would criticize it more strongly than I could, but as it is it remains an honest effort to meet many differing requirements, and it is up to each doctor to use as much of it as he can ; and when he disagrees he will be safe in thinking charitably that there has been some valid reason for the apparent oddity.—I am, etc.,

Winsford, Cheshire. W. N. LEAK.

Psychical Phenomena in Epilepsy and the Psychoses

SIR,—The article by Drs. Shafica Karagulla and E. Elizabeth Robertson (*Journal*, March 26, p. 748) expresses views with which many will be in sympathy. I feel the response of epileptic patients to drug treatment is an interesting corollary to the writers' opinions. Some anti-convulsants alleviate the mental symptoms somewhat, but they only do so in patients showing affective disorders. The more psychotic the thought content and behaviour, the less benefit there is likely to be derived from such drugs. Any change of mood is largely masked by these symptoms, whereas many patients with merely neurotic reactions improve dramatically.

The drug I have in mind particularly is primidone ("mysoline"), and these results were noted when it was first used in the epileptic wards of Long Grove Hospital, Epsom, in 1952.[1]—I am, etc.,

Croydon. DAVID J. ADDERLEY.

REFERENCE

[1] Adderley, D. J., and Monro, A. B., *Lancet*, 1953, 1, 1154.

Treatment of Vaginal Discharges

SIR,—As a taxpayer I feel the waste in the large quantities of expensive proprietary preparations which are issued to National Health patients for the treatment of vaginal discharges. As one who often sees the end-results of these cases, I deplore the frequent results of giving pessaries in quantity and without supervision.

The trouble begins, I think, with the well-meaning traveller who claims that his firm have found the cure for

the trichomonas or monilial infections, if not both. The preparation is conveniently packed up as a month's supply of pessaries or medicament (jelly or cream) and all prescribable on the E.C.10. Alas, in that month how much harm can be done. First, the preparation may be excellent, and fulfil all the claims, but in that case a small supply would have sufficed for cure. Secondly, as frequently happens, especially with sulphonamide and acetarsol preparations, the trichomonas and other infecting organisms are quickly destroyed, leaving the vagina clear for the monilia, which seems to flourish on the pessary debris, particularly those with a carbohydrate base. If this has been allowed to go on for long, the result may be a monilial infection which nothing will cure.

I feel that if only some cheap and simple glycerin or lactic acid pessaries could be ordered, to use alternating with the more patent and costly preparations, the results would be so much better. I have recently been prescribing a pessary of phenylmercuric dinaphthylmethane disulphonate with 2% lactic acid. This is a step in the right direction, as it is a combined preparation and easy to order and use. I have found it markedly more successful than the same preparation without the lactic acid.—I am, etc.,

London, S.W.4. ELIZABETH GOURLAY.

Medical Numismatics

SIR,—Although I personally can throw no light upon "Dr. Eady," I can at least add one more token to Dr. G. E. B. Payne's collection (*Journal*, March 19, p. 729).

This professional token, or more properly jetton, dates from about 1850 and was lent to me by Dr. Thomas Marmion on the occasion of the opening of the new Battersea Varicose Ulcer Clinic. Issued by John Mappin, Surgical and Deformity Instrument Maker of Newhall Street, Birmingham, it shows on the reverse side the sites of the various circumferential measurements necessary when making an elastic stocking.

Dr. Marmion tells me that these tokens of the late nineteenth century were not necessarily sanctioned by the Crown as legal tender, but nevertheless they often circulated locally and were redeemed by the originator for legal money. Thus John Mappin's token, if traded in another shop in the same street, is likely to have been accepted with the same alacrity as a farthing.—I am, etc.,

London, W.1. STANLEY RIVLIN.

The "Nape Naevus"

SIR,—The communication of Dr. F. Parkes Weber (*Journal*, March 19, p. 726) on the Sturge-Weber-Kalischer syndrome prompts us to record our observations of a condition we have come to term the "nape naevus." This abnormality consists of a cutaneous capillary haemangioma ("port-wine stain") in the region of the hair line posteriorly. The naevus may extend below the hair line, usually in a roughly triangular shape overlapping both sides of the spine, or it may be of irregular delineation and perhaps composed of separately spaced components. In some instances the naevus was confined to the area below the hair line while in others it extended upwards over the occipital region and occasionally was only visible, with careful observation, on separating the hair.

Our interest was aroused by the finding of a naevus in this situation in two patients who suffered from epileptic seizures and who demonstrated intracranial calcification of the type seen in the Sturge-Weber-Kalischer syndrome. Subsequently we came to regard the nape naevus as a concomitant of neurofibromatosis, but when our observations were extended to include a routine search of the skin hidden by the hair above the nape of the neck we became impressed by the frequency of its existence. In view of this high incidence of the nape naevus in patients not suffering from epilepsy or neurofibromatosis it is difficult to consider it as a component confined to any one particular syndrome. Some patients with the nape naevus also displayed similar naevi in other parts of the body, and, unless looked for carefully, these could readily be missed. Lastly a hereditary aspect of the nape naevus was demonstrated in several subjects. A member of the staff, for example, was able to trace its presence through three generations, the naevus in all those affected being in the nape of the neck. In one example of the nape naevus associated with fits and intracranial calcification, examination of the father showed a very extensive naevus covering almost the whole of the right side of the head but hidden from view by the hair.—We are, etc.,

J. SHAFAR.
Burnley, Lancs. A. DOIG.

Haemorrhagic Disease of Newborn

SIR,—In 1951 one of us (I. K.), with a colleague,[1] recorded the occurrence of haemorrhagic disease of the newborn presenting as a unilateral proptosis; two cases were reported with complete recovery. We now wish to record a further example of this syndrome with post-mortem confirmation of the haemorrhage situated in the orbital fossa behind the eyeball. This newborn infant died of atelectasis and also had a proptosis of the right eye. Necropsy revealed the cause of the proptosed eye as being due to a haemorrhage in the orbital fossa pushing the eyeball forward.—We are, etc.,

I. KESSEL.
Johannesburg. F. C. FRIEDLANDER.

REFERENCE

[1] Kessel, I., and Glynn Williams, C., *S. Afr. med. J.*, 1951, **25**, 126.

Exchange Transfusion in Haemolytic Disease of the Newborn

SIR,—We have read with very great interest and benefit the excellent paper on the above subject by Drs. William Walker and G. A. Neligan (*Journal*, March 19, p. 681), and from our small experience in the Ronkswood Hospital unit find ourselves in complete agreement with them on many points. We have, however, found that, in spite of the most careful maintenance and the use of silicone fluid, syringes do tend to stick from time to time. We have found that the simplest solution to this problem is to have half a dozen syringes in our emergency exchange transfusion set. We have found that as many as six may be required during the course of an exchange of 500 to 600 ml.—We are, etc.,

J. A. CHALMERS.
Worcester. C. J. THORNBERRY.

Treatment of Coughs

SIR,—The whole trend of your leading article (*Journal*, March 12, p. 651) is that the treatment of cough should be by sedative cough mixtures; you apply this especially to patients who "seek advice about a cough which has persisted for more than a short time" and whom you consider it "clearly desirable to examine carefully." Sir, in general practice we rarely prescribe for coughs of even short duration without careful examination; serious acute disease may frequently only have been present for a short time and the patient still ambulant when he first consults us, but I will not dwell on that now since I have not access to the paper concerned, on the experiment of giving three grains of codein to suppress cough, though I should scarcely like to repeat it.

When I first joined the wartime R.A.M.C. my regular colonel quoted to me an old regulation of the Service which, so he said, laid down "Mist. expect. sed. will be prescribed for not more

than two days; after that mist. expect. stim. will be prescribed." I regret the clinical interference, but I still think this was good advice and probably saved many lives and much invalidism; patients have frequently come to me with persistent minor bronchial catarrh treated for too long with sedative mixtures and very quickly relieved with pot. iod., and pot iod. only. I have seen a fellow patient in hospital dying of Gee's linctus every four hours. From a personal point of view I have frequently obtained great relief with a single dose of pot. iod., though a similar effect may be obtained by the ingestion of large quantities of hot tea—embarrassing if one is short of breath, and not always convenient to work or sleep. I believe antispasmodics, very valuable in moderation, can have the same deleterious effect as sedatives when given in excess, since I suspect "normal spasm" may have some physiological action in extruding the sputum.

I agree that in severe advanced chronic bronchitis pot. iod. is of little or no value, but I suggest that sedative mixtures are dangerous to these patients when lack of sleep at night outweighs their disadvantages. At least pot. iod. does little harm if the patient likes a cough bottle, and one can ring the changes on hot fluids, postural coughing, inhalations, antispasmodics, local heat, and antibiotics—anything but sedative cough mixtures. It should be remembered that many patients given a relatively strong linctus will take too much unless very specifically warned. Anyone can *suppress* most coughs, just as anyone can *suppress* most pains with opiates, but this would hardly be regarded as the practice of medicine. You appear highly optimistic in regarding a clinical trial of linctuses in cough—a subjective symptom unless one lives with the patient—as easy. I feel it would be neither easy nor particularly useful. Further research into the mode of action of potassium iodide in troublesome but not advanced bronchial catarrh and in asthma, and search for new and more effective sputum liquefiers, would be more helpful.

Sir, only a strong sedative could control my indignation and I make no apology for my views, those of one of the 10,000 or so G.P.s who have been treating "cough" every day for 16 years, in other words "cough specialists." I hold no brief for senega, ammonia, liquorice, chloroform, squill, syrup of Virginian prune, or any of the other deleterious substances sometimes advocated. Let others defend them.—I am, etc.,

Amble, Northumberland. R. P. ROBERTSON.

Cancer Education

SIR,—The paper by Drs. J. Walter and E. C. Atkinson (*Journal*, March 12, p. 627) describing an early cancer detection and educational scheme in general practice reveals that, of 1,482 presumably healthy list patients, no fewer than 837 (56%) accepted an offered free medical examination, the purpose of which was to detect early cancer. The fact that one new case of (metastasizing) cancer was discovered is noteworthy, but the really interesting feature of this experiment is the amazingly high number of volunteers, which in itself conflicts with the theory that many people are afraid of cancer detection.

Hull, a city of 300,000 inhabitants, has been taken over by the cancer educationalists as a suitable experimental centre and we are constantly bombarded with British Empire Cancer Campaign lectures and leaflets on the subject. Also, we can listen to recorded cancer talks by merely dialling a number on the local telephone system, and, since these talks are given in serial fashion, we have the opportunity to apply to the Marie Curie Memorial Foundation for the scripts of any previous talk we may have missed. The Kingston-upon-Hull Corporation has now entered into the spirit of things with a huge notice in the local newspaper telling the "facts." To an intelligent man with an interest in the subject, the collected facts are really a series of warnings. He is urged to watch for ulcers and lumps in skin, lip, mouth, and throat, etc.; he is told to watch his stools and urine for blood; to watch out for hoarseness and dysphagia. The ladies are advised to search their breasts for lumps (not more than once every 3 months) and to keep a careful watch on their menstrual cycles. And, of course, if ever in doubt we are all urged to consult our doctor.

Your leading article on this subject (p. 652) states that there is need for some cancer education of the public, having satisfied yourselves that the main criticisms against it—that surgeries would be crowded with worried people and that cancerphobia would be created—are disproved by the experiment in cancer education carried out by Dr. Ralston Paterson and co-workers.[1] Such an assumption is surely premature. The huge business concern did not become huge after its first few advertisements; nor was the enormous incidence of bowel sickness created by the initial advertisements for purgatives. In any case, the Ralston Paterson experiment was carefully controlled and confined itself to certain neoplasms (breast excepted) almost certainly readily curable in the very early stages of the disease. Here in Hull we have propaganda directed against certain neoplasms extremely difficult to cure at any stage of the disease—bladder and oesophagus, for example. For that matter, what is an early neoplasm? Duration of lump is not by any means necessarily tied to stage of disease. Breast, so popular with the educationalist, is notorious in this respect. Even the better-behaved neoplasms, such as cervix, are often advanced and quite incurable in spite of a short history of bleeding and vice versa. What about those unfortunate women who are told to feel their mastitic breasts? It is difficult enough for the experienced clinician to make a diagnosis readily, without biopsy. Once the public do start taking notice it would be most unfortunate if any doctor were to miss an early cancer after the patient has presented it on a plate, so to speak. All such patients will be pushed on to the hospital consultant, who would not dare to turn away any lump, however innocent, without biopsy or local excision.

Is it really necessary? Is there any reason to suppose that doctors to-day die less frequently of this disease than do other professional groups? The V.D. campaign during the war was well worth while for the very reason that quick cure could be offered the patient in practically every case; but in the present state of our knowledge cancer education, on any large scale, is merely putting the cart before the horse.—I am, etc.,

Hull. K. W. BEETHAM.

REFERENCE

[1] Paterson, R., *et al.*, *British Medical Journal*, 1954, 2, 1219.

Neon Lighting in Hospitals

SIR,—I would like to support the plea of Dr. W. B. Bacon (*Journal*, March 12, p. 666) for the abolition of neon lighting in anaesthetic and recovery rooms and operating theatres. With this form of illumination it is quite impossible to detect minor degrees of cyanosis, despite the asseverations of the manufacturers to the contrary. I already know of an anaesthetic death from unrecognized anoxia in a patient undergoing herniotomy under spinal analgesia.

The introduction of strip lighting in modern hospitals is an unfortunate example of a tendency which is becoming all too common in medicine: the assumption that because a thing is new it must be good.—I am, etc.,

London, W.1. MASSEY DAWKINS.

Doctors' Visits and Coronary Infarction

SIR,—There have been an article and a letter lately in the *Journal* (February 5, p. 318, and February 26, p. 539) about patients suffering from coronary infarction dying shortly after being seen by the doctor. Your correspondent seems to think that this occurrence is more or less confined to hospital in-patients. However, it can also happen when visiting a patient in his home, as an experience of mine testifies.

I was asked to see a man who had been rather ill in the night with chest pains and attacks of dyspnoea. These symptoms undoubtedly were due to coronary insufficiency. In all probability he had a coronary infarction. There was a history of "bad heart" for years, made worse by chronic bronchitis. Also he had been suffering from hypertensive symptoms. His age was approximately 68 years. He was much better on the following morning when I called to see him. There are two points worth noting which I think are

more important than any details of clinical examination—that is, the fact that he was deaf and I had to shout to make him hear, also the fact that I questioned his self-diagnosis of "bad heart." His wife thought that he was rather upset by my questioning his diagnosis. Also she seemed to think that I need not have shouted quite so loudly. At all events I learned later that the patient, although quite comfortable when I left the house, died a few minutes later. I also learned subsequently that the deceased was a sensitive type of person rather easily upset.

In future I shall speak softly to all patients, whether deaf or not. Also I think it is as well to agree with any opinions that they may express.—I am, etc.,

M. B. BARRY.

Melanoma and Pregnancy

SIR,—Dr. H. Stewart's statement (*Journal*, March 12, p. 647) that "no reference is found to the effect of pregnancy on the growth of a melanoma" calls for comment. Pack and Scharnagel[1] have suggested that "every prenatal examination of the mother should include a survey of her pigmented moles, and those subject to irritation, as well as any situated on the genitals or feet, should be removed and histologically examined." Cunningham[2] writes that, because of the unusual rapidity with which melanomata grow and metastasize in pregnancy, prime consideration must be given to prophylaxis. The stimulant is, of course, the melanocyte-stimulating or melanophore-expanding hormone of the pituitary, the secretion of which, according to Lerner *et al.*,[3] increases progressively from the eighth or ninth week until term, after which it reverts to normal in a few days. Nevertheless, therapeutic abortion is said to have no effect in checking the growth of melanomata.

The melanophore-expanding hormone is also responsible for the enlargement of lentigines or for the appearance of new ones in some patients receiving treatment with corticotrophin. It seems clear therefore that hormonal influences are of the greatest importance in the activation of melanomata, as witness the benignity of these lesions before puberty.—I am, etc.,

London, W.1. BRIAN RUSSELL.

REFERENCES

1 Pack, G. T., and Scharnagel, I. M., *Cancer*, 1951, 4, 324.
2 Cunningham, J. A., in *Progress in Fundamental Medicine*, 1952, edited by J. F. A. McManus, p. 28. Kimpton, London.
3 Lerner, A. B., *et al.*, *J. clin. Endocr.*, 1954, 14, 1463.

POINTS FROM LETTERS

Chilblains

Dr. W. M. GRAY (Cults, Aberdeenshire) writes: Your annotation (*Journal*, March 5, p. 592) prompts me to send the following prescription, my use of which is purely empirical. In every case in which I have prescribed it the results have been very satisfactory and the patient has been relieved of the sores (open) and pain and discomfort. . . . I copied the prescription from the *British Medical Journal* many years ago and it has done all it claimed. Perhaps it may improve the circulation and is so simple: pot. cit. 15 gr. (1 g.), sod. bicarb. 10 gr. (0.65 g.), inf. gent. 2 dr. (7 ml.): 2 dr. (7 ml.) three times a day to be taken at very beginning of itching or other symptom.

Night Cramps

Colonel P. F. CHAPMAN (Taynuilt, Argyll) writes: I was interested in the annotation on night cramps (*Journal*, March 12, p. 653), having myself been a sufferer. I was surprised to find no mention made of what I have found in my own case, and in that of others to whom I have recommended it, an infallible preventive and cure. It is to take a few mouthfuls of strong salt and water before turning in at night. My last meal often consists of porridge, and I find by oversalting this the same end is attained. . . . I have found myself, as pointed out in your annotation, that night cramps occur after heavy exercise such as marching and drill, or now, in my own case, after a long day's walking over the hill after game. This method of prevention and cure is a very simple one, and I feel sure will prove efficacious in a very large number of cases. The administration of saline either by the mouth or into the blood is now routine in cases of heat stroke.

Obituary

H. M. J. PERRY, C.B., O.B.E., F.R.C.P.

The death of Major-General Marrian Perry occurred at his home at Walton-on-Thames, where he had been living in retirement for some years, on March 23, 12 days after his 71st birthday.

Henry Marrian Joseph Perry was born at Cork on March 11, 1884, and was educated at Queen's College (now University College), Cork, qualifying L.R.C.P.&S.I. in 1906. Commissioned in the R.A.M.C. in the following year, he served in China as a young man, but had returned to home service well before the outbreak of the first world war in 1914. He went to France with the original British Expeditionary Force and was made prisoner of war during the early period of hostilities.

[*Lafayette*

It was after repatriation that Perry began his career as an Army pathologist, and he finished his war service with a rising reputation. At the end of the war Leishman began his reorganization of the Army pathological services, and, recognizing Perry's great ability, posted him to the Royal Army Medical College, Millbank, where he was to spend so many years of his professional life, and where he was appointed professor of pathology in 1922. In 1926 he was seconded to the Foreign Office to serve as director of the Egyptian public health laboratory service, with his headquarters in the Cairo central laboratory. It was a responsible post with quite wide terms of reference, and Perry proved to be a good choice.

In 1930 he returned to the Army to take up a further period as professor at Millbank, and later was promoted to hold the combined appointment of professor and director of pathology, a post he continued to hold until the second year of the second world war, after which he retired from the Army and gradually gave up professional work altogether. For his services in the first world war Perry was appointed O.B.E. in 1919, by which time he had attained the rank of major, and for his work at Millbank he was appointed C.B. in 1937. Promoted full colonel in 1934, he became major-general in the following year. He was an Honorary Surgeon to the King from 1933 to 1940, and he was elected F.R.C.P. in 1941. He is survived by his widow, formerly Miss Mary E. Brewer, whom he married in 1912 and to whom we extend our sympathy.

We are indebted to Lieutenant-Colonel H. J. BENSTED for the following appreciation: Perry will best be remembered by senior and retired officers of the R.A.M.C. for his pathology and bacteriology lectures in the junior and senior courses of instruction at Millbank, but those who worked closely with him knew him for a most painstaking technician and a reliable bench worker. He took a great deal of trouble over everything that he set out to do. In order to make himself certain of delivering without notes an unhesitating and word-perfect lecture, he used to learn

his carefully prepared script and then declaim it silently as he walked round and round the lake of St. James's Park. These efforts were not wasted, for his lectures were very widely appreciated. Perry had a strong personality, but he also had a good deal of charm and could carry a committee without obvious effort. He was quick to see the importance of any scientific development that might be of importance to the health of the Army, and the encouragement that he gave to the investigations that led to the improvement of the Army T.A.B. vaccine and the introduction of active immunization against tetanus are witness to this. Perry was always well served, but the development of the Army pathological services in the second world war owed much to his own foresight and organizing ability.

R. G. LADKIN, M.B.E., B.M., D.P.H.

The sudden death from poliomyelitis of Dr. R. G. Ladkin on March 14 at the age of 36 has cut short a career of the highest promise and deprived Uganda of the services of an outstanding medical officer. To those privileged to know him he will be remembered as the ideal Colonial medical officer. Able, resourceful, adaptable, he seemed to be filled with boundless energy and was always willing and co-operative, and interested in every aspect of medical work in East Africa and in many fields outside medicine. He had a vivid personality, and was that forceful, formidable man, a truly realist Christian idealist. He knew only too well the frustrations and difficulties of medical work in Africa, the immense problems, the meagre resources, but he never let them daunt or deter him, and he flung himself cheerfully and selflessly into the task of improving the life and health of the African people of Uganda.

Ronald Greaves Ladkin was born on January 13, 1919, and was educated at Kingsbridge Grammar School and at Exeter College, Oxford, where he was Stapledon Scholar and Devon Scholar, taking the B.M., B.Ch. degrees in 1942. After a period as house-physician at the Radcliffe Infirmary he entered the Colonial Medical Service in 1943 and spent some years in the more remote districts of Uganda before being posted to Kampala, where he taught anatomy in the medical school of Makerere College and carried out much surgery at Mulago Hospital. He became interested in genito-urinary surgery, and this led him to a special study of venereology, which in turn led him towards public health. He took his D.P.H. in 1948 and visited Trinidad to study venereal disease control. On his return to Uganda he was given the medical charge of Mengo District and later of the Province of Buganda. This included the peri-urban African areas around Kampala, in whose problems he became deeply interested and of which he gained a vast knowledge. This post entailed much safari work, at which he was an expert and in which he took great pleasure. His clinical acumen, which he retained to the full, led him to the discovery that the so-called pygmies of the Mabira Forest were in fact pathological dwarfs. It also caused him to institute an improved system of dispensary returns so that he was able to analyse the causes of African morbidity. All the information he collected and the knowledge he gained were generously shared with his clinical colleagues: he lectured to medical students, and frequently spoke at meetings and conferences of the British Medical Association in Uganda. This willingness to help others is gratefully remembered, and it is a sad blow that the frequent concluding remark—"Ask Ron Ladkin—he's sure to know"—will never again elicit his generous help. One of his greatest assets was his knowledge and understanding of the African mind and his ability to persuade Africans to co-operate with him. In part this was because they recognized his curative skill and were the more willing to accept his advice on prevention. His work in Buganda led to great improvements in many fields of public health and attracted the attention of medical visitors from other countries. His colleagues watched his activities with admiration and respect, and his appointment as M.B.E. in 1952 for his work in Buganda gave them much pleasure.

Ronald Ladkin had become more and more convinced of the necessity for health education in Africa, and he took up this problem with his usual enthusiasm, using many new techniques of his own devising. His success in this field was so outstanding that he was transferred to medical headquarters at Entebbe, where a new post, that of senior medical officer in charge of health education, was created for him, and his sphere was widened to include the whole Protectorate. In this capacity he travelled ever more widely. He spent much time and worked very hard in detailed planning and had interested many different bodies in this task. All his plans, which were coming to fruition when his untimely death took place, will go forward as he would wish, but his zeal and energy will be sorely missed and years will pass before another medical man can gain the detailed knowledge of the health problems, especially of the peri-urban areas, which Ladkin possessed.

Just as his official life was full, happy, and rewarding, so was his unofficial. He was active in the affairs of the Red Cross. He was a founder and past president of the Uganda Mountain Club, and spent many happy hours climbing and exploring, especially in the Ruwenzori mountains. He enjoyed playing cricket and would cheerfully hurl down fast balls for long spells under the hot African sun. Shortly after going to Kampala he married a nursing sister of the Colonial Nursing Service. His home life was ideally happy, and his wife ably supported all his work. Everywhere they went they set themselves to create a beautiful garden ablaze with colour. He lies under the green grass and the blue skies of Entebbe within sight of Lake Victoria. Uganda and his colleagues there have lost a great servant and friend they could ill afford to lose. The sympathy of all their friends goes to his widow and three young children in their great loss.—J. N. P. D.

F. H. SCOTSON, M.B., F.R.C.S.

Mr. F. H. Scotson, one of Manchester's leading surgeons, died on March 23 at the age of 55.

Born on January 28, 1900, at Manchester, where his father, Dr. F. C. Scotson, was a well-known general practitioner, Frederick Hector Scotson was educated at Manchester Grammar School and at Manchester University. He had a distinguished record as a medical student and was awarded numerous prizes and distinctions, including the Bradley Memorial Scholarship in surgery and the graduate prize in medicine. In 1922, in his 23rd year, he obtained medical degrees from both the Manchester and London universities, being awarded honours in his final examination at Manchester. In the following year he took the London Conjoint diploma, and in 1924 passed the final examination for the F.R.C.S., but, being under age at the time, did not qualify to receive the diploma until the following year. After graduation he was appointed house-surgeon at Manchester Royal Infirmary, the first of a long series of

appointments to that hospital: he was resident surgical officer from 1927 to 1929 and later surgical officer to out-patients and surgical tutor. During this period he took the opportunity to visit some of the American clinics. In 1930 he was appointed honorary surgeon to the Manchester Northern Hospital and to the Manchester Victoria Memorial Jewish Hospital, and a few years later he became consultant surgeon to the Crumpsall Hospital.

Scotson was a general surgeon with his chief interest in the surgery of the abdomen. He published a number of papers in this and other journals and spared no pains to keep abreast of current surgical ideas. He was a keen and good teacher and for the past seven years had been a lecturer and examiner in surgery in Manchester University. At the time of his death he was president of the section of surgery of the Manchester Medical Society and was to have given his presidential address on the subject of peptic ulceration. He was a past president of the Middleton and North Manchester Medical Society and a former vice-president of the Manchester Pathological Society. He was twice married: first, in 1928, to Annie M. Bradbury, who died in 1940, and second, in 1942, to Leila M. B. O'Connell, who survives him, together with her son and the two sons and one daughter of his first marriage.

R. L. H. writes: F. H. Scotson was an excellent technician and a shrewd clinician. In addition, he was always extremely kind to and thoughtful of his patients. He led a very active professional life, for besides a heavy hospital programme he had an extensive private practice. His friends had told him he was working far too hard, and unfortunately their prophecy proved true, for the constant nervous strain under which he was working precipitated a breakdown which never satisfactorily cleared up. A remarkably tolerant man, he had, in addition to his professional ability, many endearing personal qualities. His natural friendliness was apparent to all, and as "Scottie" he will be remembered and his loss mourned by all his colleagues in Manchester. His patients have lost not only a good surgeon but a friend.

Dr. NEIL MCLEAN died on March 14 at Ryde, Isle of Wight, where he had been in practice for the past eight years. A native of Skye, Neil McLean was born in 1898, and he graduated M.B., Ch.B. at Glasgow University in 1924, after seeing active service with the Cameron Highlanders in France, the Balkans, and Russia in the first world war. At the university he was a well-known shinty player, gaining his blue. He joined the Colonial Medical Service in 1926, and served in Kenya for twenty years, retiring as senior medical officer in 1946 after a severe illness.

P. R. writes: Neil McLean did valuable work in Kenya, especially in sleeping sickness research, for which he was awarded the North Persian Forces Memorial Medal in 1931, an award given for the best piece of original work in tropical medicine for the year. For a time he was stationed in the Masai Reserve, and when he was posted elsewhere the Masai tribe offered the Government a large number of their precious cattle to have him back again, probably a unique tribute to a doctor and an index of the affection with which natives of all the Kenya tribes regarded him—an affection shared by the European population, officials and settlers alike. Neil will long be remembered by all who knew him, and their sympathy goes out to his wife and three daughters. In 1935 he married Miss G. Davidson, of Whitley Bay, who proved a constant support and strength to him. His was a lovable personality, and his cheerfulness and courage in adversity won the admiration of his friends. I can see him now sitting with his microscope at a camp table under a thorn tree on the shore of the Nyanza, talking Luo to his patients with a strong Gaelic accent, or, dressed in an old kilt, fishing from a boat in Broadford Bay, singing quaint Gaelic airs. Though greatly incapacitated by cardiac trouble, he took up practice in Ryde in 1947, where he continued, making a brave fight against declining health, until his death at the early age of 56.

Medical Notes in Parliament

Radioactive Contamination Report

Mr. ARTHUR HENDERSON (Rowley Regis and Tipton, Lab.) asked the Prime Minister on March 29 if he would publish a White Paper containing all available facts and information, together with the report from British scientists, on the effects of continuing radioactive contamination of the world's atmosphere.

Sir WINSTON CHURCHILL stated that the Government had already invited the Medical Research Council to review the existing scientific information on the medical aspects of nuclear radiation and to prepare a report. The report would cover the medical aspects of nuclear radiation, including the genetic aspects. It would review existing scientific information and set forth the most up-to-date information and the latest research results available. The report would be laid as a White Paper.

London Atmosphere Measurements

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) asked the Parliamentary Secretary to the Ministry of Works (as representing the Lord President of the Council) on what evidence his estimate was based that there was no significant increase in the radioactive content of London's atmosphere during recent years. Mr. J. R. BEVINS told him that it was based on measurements made in London periodically since 1947. Dr. STROSS said that M.P.s who went to the Chester Beatty Research Institute, as members of the Parliamentary and Scientific Association, were informed that the radioactive contamination of the London atmosphere was 10 times as high now as when measurements first began, and was 300 times the normal during the great fog of 1952. Was that taken into account, could it be checked, and would it not be significant? Mr. BEVINS replied that he had checked the statement in Dr. Stross's pamphlet that the radioactivity had increased 10 times. There must have been a misunderstanding during the visit to the Institute, because he was assured that the increase in radioactivity since 1947 had been negligible. It was true that the measurements that were taken were very limited, and the evidence was not conclusive in its present form. Nevertheless, he would like to refute the statement that there had been a large increase in radioactivity. Dr. STROSS asked him to check that point with the Chester Beatty Institute, and make certain that the facts given to those who were present were as he had stated. Mr. BEVINS said that the Lord President had checked with the Institute. The Institute denied that the statement was made, and said that if such a statement were made there had been a misunderstanding on one side or the other.

Hospital Workers' Protection

Mr. S. SWINGLER (Newcastle-under-Lyme, Lab.) asked the Minister of Health on March 28 what regulations he had issued about the protection of hospital workers using radioactive substances and about the disposal of radioactive waste in hospitals. Miss PAT HORNSBY-SMITH, Parliamentary Secretary, said that it was the normal practice of hospitals in the Health Service to observe the recommendations of the British *X*-ray and Radium Protection Committee about protection and working conditions in *x*-ray and radium departments. This code of practice was, however, in some

respects out of date, and the Minister hoped to bring into operation shortly a revised code approved by the Radioactive Substances Advisory Committee which included a section governing the disposal of radioactive waste.

Charges Against M.R.C. Denied

Mr. PETER FREEMAN (Newport, Lab.) asked the Parliamentary Secretary to the Ministry of Works, as representing the Lord President of the Council, whether he was aware that a number of cases had recently been brought to the courts of cat-stealing on a large scale and that several people had been convicted for this offence; that these cats had been stolen for sale to medical research laboratories, as admitted in court; that the cost of the defence and the fines had in some cases been paid by the M.R.C. and that they had employed the same counsel in most of the cases; what authority existed for the payment of such expenses out of public funds; how much had been spent on each of these cases in the last six months; and what action he proposed to prevent a recurrence of such incidents. Mr. BEVINS, replying on March 29, stated that he was glad to have the opportunity of stating, quite unequivocally, that there was no truth whatever in the hon. Member's allegations against the M.R.C. Mr. FREEMAN said that further inquiries should be made. Counsel who defended these cases was known to have made a voluntary statement that the fines and costs had been paid either by the M.R.C. or one of its members. This was confirmed by a Mr. Taylor, of Rectory Square, London, E.1, who supplied over 100 cats a week—most of which had been stolen—to the M.R.C. The same counsel was employed to defend Mr. Taylor, and had been employed on repeated occasions. Some brothers named Bailey were recently ordered to pay £170 in fines and costs, and they had admitted that in that case the cats stolen had been sent direct to the M.R.C. Mr. BEVINS said that the Lord President of the Council had been into the matter with meticulous care, and was satisfied that none of the suggestions in the question was based on evidence. The barrister whose name was supplied to him had had no contacts of any sort with the M.R.C. As for statements made in court, defendants sometimes told the truth and sometimes they did not. Mr. FREEMAN gave notice that he would raise the matter again.

Doctors' Telephones

Mr. D. WALKER-SMITH (Hertford, Con.) asked the Minister of Health on March 28 whether he would seek powers to ensure that general practitioners in the Health Service should be available to their patients on the telephone. Mr. IAIN MACLEOD replied "No," but added that, without prejudging any entirely exceptional case, it seemed quite clear to him as a general matter of common sense that a doctor providing general medical services was not in a proper position to fulfil his obligations to visit his patients when their condition so required if he did not make reasonable arrangements for them to communicate with him by telephone.

Foreign Patients in Hospitals

Mr. A. HURD (Newbury, Con.) asked if the Minister of Health would make a sample check of admissions to hospitals to show the numbers of patients who were not ordinarily resident in the United Kingdom, and to find out how many had come here with the purpose of obtaining free hospital treatment. Miss PAT HORNSBY-SMITH, Parliamentary Secretary, replied on March 28 that the Minister was not satisfied that the information obtained would be of sufficient value to justify the very considerable work which would be involved.

Progress in Leprosy Treatment

Mr. W. TEELING (Brighton, Pavilion, Con.) on March 30 asked the Secretary of State for the Colonies how many leper hospitals there were in the Colonies, where they were, and in what Colonies lepers were refused permission, even when suitably accompanied, to visit towns away from the leper centres. Mr. H. HOPKINSON, the Minister of State, Colonial Office, stated that there was an institution for the treatment of leprosy in every Colony in which the disease was endemic, either in leprosy hospitals, out-patient departments of general hospitals, or in separate settlements or villages. Contact with the general public in the case of patients under treatment was related to the risk of infection in each case. Mr. TEELING said that recent discoveries had led those studying the disease to consider that it was no longer necessary to have completely isolated settlements. Would the Minister make sure that the Colonial Office was keeping that in mind? Mr. HOPKINSON said he entirely agreed. Many of the new drugs had made it possible to treat an increasing number of cases as out-patients, to allow patients in institutions to go home for short periods, or to discharge them altogether.

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) asked if we may take it that it is now accepted that leprosy is not a dangerously infectious or contagious disease, and that free movement does not necessarily bring danger to the community. Mr. HOPKINSON replied "Yes." The danger depended on the specific case, but in a general way people still retained a serious dread of the disease. Only education on the effects of modern drugs and so on would eradicate that fear.

Mr. TEELING also asked how many lepers were on the leper station near Fiji; what had been the expenditure on this leper island over the last five years, year by year; and how many of the lepers there were European, Fijian, and Indian, respectively. Mr. HOPKINSON informed him that there were 634 patients in the Fiji Leprosy Hospital at Makongai. Expenditure in Fijian pounds was 51,000 in 1949, 55,000 in 1950, 58,000 in 1951, 69,000 in 1952, and 64,000 in 1953. Three of the lepers were Europeans, 139 Fijians, and 193 Indians. Mr. TEELING asked if it would be possible to bring those people back into Fiji and Suva. The leper island was far away, and the lepers felt completely cut off. Mr. HOPKINSON said he would refer the suggestion to the Governor of Fiji. He added in answer to Mr. T. L. IREMONGER (Ilford, North, Con.) that Gilbertese, Samoans, Cook Islanders, and others were also treated in the colony. Generous help had been given to the hospital from the New Zealand Leper Trust Board and others.

Blood Tests for Motorists

Mr. S. P. VIANT (Willesden, West, Lab.) asked the Minister of Transport on March 30 whether he was aware that a majority of the public were in favour of the imposition of a blood test for motorists involved in serious accidents; and if he would give consideration to the introduction of legislation to enable such tests to be carried out in the future. Sir F. MEDLICOTT (Norfolk, Central, Nat. Lib. and Con.) asked if, in view of the recent substantial increase in the number of deaths and injuries on the roads, the Minister would make legislative provision for the imposition of a blood test on all drivers of motor vehicles involved in accidents causing death or serious injury. Mr. JOHN BOYD-CARPENTER, answering them both, said that he had no evidence either to confirm or to reject the assertion made by Mr. Viant. Research was being carried out jointly by the Medical Research Council and the Road Research Laboratory to find out, under laboratory conditions, how precisely measured quantities of alcohol affected driving performance and whether such effect could be satisfactorily assessed. He hoped their report would be available this year.

Mr. VIANT said that his question was based on evidence provided by a recent Gallup poll conducted by the *News-Chronicle*. Sir F. MEDLICOTT said the reliability of this test had been largely proved—which provoked cries of dissent—and it would be a much more satisfactory way of ascertaining the condition of drivers than the present tests of conduct. Mr. BOYD-CARPENTER said that he would rather await the conclusions of the Road Research Laboratory tests. Mr. R. R. STOKES (Ipswich, Lab.) said that most M.P.s

would fail to pass such a test immediately after lunch, and it bore no relation whatever to the condition of the driver.

Doctors' Lists.—The average number of patients on doctors' lists on July 1, 1954, was 2,219 in England and 2,077 in Wales. In July, 1951, the numbers were 2,391 and 2,348 respectively.

Cortisone Products.—The Minister of Health is not yet in a position to make cortisone products available on prescription by general practitioners.

Medico-Legal

£2,000 DAMAGES FOR SILICOSIS

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

On March 25, 1955, a majority of the First Division of the Scottish Court of Session upheld an award by Lord Wheatley to John Harkness Wardlaw of £2,000 damages.[1] Wardlaw had sued his employers, Bonnington Castings, Ltd., for damages for lung injuries sustained through inhaling silica dust during his employment as a steel dresser from January, 1942, until May, 1950, when he was found to be suffering from pneumoconiosis. It was Wardlaw's job to operate a pneumatic hammer in the dressing shop to remove steel rags from castings.

Wardlaw's case was that his pneumoconiosis was caused by a breach of duty by his employers to take reasonable care for his safety, among other things by failing to provide employees in the dressing shop with masks or respirators to intercept the dust, and that such masks were a simple and inexpensive precaution which was frequently adopted in the foundry industry.

Lord Carmont, dismissing the appeal, said it would not do for the employers to say that it was much more likely that the disease was contracted through work at a hammer close to the source of dust rather than from breathing the air of a shop which was generally contaminated. Even if most of his inhalations took place near the source of dust, a minority of inhalations from the general atmosphere of the shop needlessly contaminated through breakdown of the extractors might well have contributed a quota of dust to Wardlaw's lungs and so helped to produce the disease. The evidence did not show that in 1950 a mask or respirator was in common use, but the employers had failed to show that silica dust from sources other than the hammer had played no part in causing the disease.

Lord Russell, agreeing with Lord Carmont, said that, having anxiously considered the evidence, he was of opinion that the employers had not discharged the onus resting on them.

The Lord President, Lord Clyde, would have allowed the appeal. In his dissenting judgment he said that, although an effective mask would have prevented the inhalation of the particles of silica dust loosened from the surface of the casting by the hammering operation, the evidence showed that in 1950, in spite of considerable research and effort by Government and departmental committees, no such respirator or mask existed. In his view the evidence did not show that the breakdown in ventilation had any causal connexion with Wardlaw's disease, and Wardlaw had failed to discharge the onus that it had. In his view the ventilation breakdown had been the employer's only breach of duty, and it was not shown that its effects had caused the disease.

SURGEON WINS FEE CLAIM

Judge W. H. Paton gave judgment for an orthopaedic surgeon at Bristol County Court on March 28 against a woman dancing teacher who alleged that the surgeon had forced her to walk on a broken ankle. The judge said he could not accept her story and entirely exonerated the surgeon. The judgment, with costs, was given to Mr. Kenneth H. Pridie, of Clifton, Bristol, on his claim for £48 6s. for his professional services rendered to 56-year-old Mrs. Mary Ellen Boss, of Bristol. A counter-claim by Mrs. Boss for damages for alleged negligence was dismissed.

Mrs. Boss, a dancing instructress, said she broke her ankle in October, 1949, and Mr. Pridie set it in plaster. The next month she went to his surgery. He took her sticks away from her and insisted that she was only suffering from nerves. He told her to walk the length of the room to the *x*-ray table. She said that Mr. Pridie told her friend and partner, Miss Hilda Walker, who was with her at the time, to go home for Mrs. Boss's other shoe, so that she could walk home. "He removed the plaster and manipulated my foot, with great pain to me, and said my ankle was perfect," and that she would dance as well as ever she did. Mr. Pridie went outside, but then rushed in and said, "Don't put that foot to the ground. If you do you will be a cripple for life." Mrs. Boss said she replied, "You are too late. You have made me walk already." She said she went home in an ambulance.

Mr. Kenneth Pridie, a consulting orthopaedic surgeon to several hospitals, said that before ever he saw Mrs. Boss he examined the radiographs which had been taken at Bristol Royal Infirmary. He realized that she had a very severe fracture of the ankle, which was bound to produce a permanent disability whatever treatment she had. He gave her an injection into the ankle and a sedative, manipulated the bones, and put on a plaster. Dealing with the events at his surgery in November, 1949, Mr. Pridie said he sent Miss Walker for the shoe before he had examined Mrs. Boss, but when he did so he found that the ankle was unstable. It was not until five years later that he first knew it was being alleged that he had compelled Mrs. Boss to walk on the ankle. He had no complaint from her that day about anything. She was very emotional and he did his best to comfort her.

Judge Paton, giving judgment, pointed out that Mr. Pridie eventually performed an operation on Mrs. Boss. It was very difficult, he said, to believe that a person who had really been treated as she says she had been treated by Mr. Pridie would have allowed him to go on treating her. It has never been suggested that she even considered anybody else doing it. He was quite unable to accept her story. No doubt she became extremely despondent and upset, and had persuaded herself that she was badly treated by Mr. Pridie. The judge was completely satisfied that, so far as Mr. Pridie was concerned, there was nothing in his conduct of this case with which he should reproach himself.

The Medical Defence Union instructed Messrs. Hempsons, solicitors, to act for Mr. Pridie.

[1] *Scotsman*, March 26, 1955.

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on February 26 the degree of D.M. was conferred on J. F. D. Frazer and A. L. Turnbull.

Dr. E. M. Vaughan Williams has been elected to an Official Fellowship at Hertford College.

In Congregation on March 8 the appointment of Dr. D. St. C. Roberts as a Clinical Tutor in Ophthalmology from April 1, 1955, to September 30, 1957, was approved.

James Learmonth Gowans (Lincoln College) has been elected to the Philip Walker Studentship in Pathology for two years from October 1, 1955.

ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH

At a quarterly meeting of College held on February 1, with the President, Sir Stanley Davidson, in the chair, the following were elected Members of the College:

G. J. Summers, A. Muir, D. P. Puri, L. E. Wynter, S. Bell, A. K. Black, M. B. Morris, J. A. Kay, I. M. Cuthill, D. C. Peiris, T. S. Kalyanam, P. S. Macfarlane, H. M. P. Perera, F. V. Edrisinghe, D. M. Chakraborty, V. Srinivasan, P. M. Hewlett, G. F. Trobridge, B. Kaplan, E. D. Myers, M. S. Karve, H. S. Wong, T. A. Cunningham, D. C. Sen, F. O. Simpson, C. G. Caro.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **March 19** (No. 11) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	10	0	3	0		18	2	5	0	2
Dysentery	1,816	195	321	16	1	1,124	125	276	11	10
Encephalitis, acute	0	0		0		4	1			
Enteric fever:										
Typhoid	2	0	0	0	1	2	2	0	0	
Paratyphoid	7	0	0	0	0	45		0	0	
Food-poisoning	117	10		1		159	18		3	
Infective enteritis or diarrhoea under 2 years				12	7				13	26
Measles*	29,018	3685	374	583	93	2,325	57	107	49	428
Meningococcal infection	48	4	22	1	2	36	3	11	2	1
Ophthalmia neonatorum	33	4	4	0		41	3	4	0	1
Pneumonia†	980	58	257	42	18	704	39	220	1	7
Poliomyelitis, acute:										
Paralytic	10	2	1	0	1	13	0	2	0	
Non-paralytic	3	0				6	1			
Puerperal fever§	252	43	9	0		262	34	7	2	
Scarlet fever	839	42	88	61	19	1,282	41	144	36	32
Tuberculosis:										
Respiratory	688	71	139	25		790	97	192	16	
Non-respiratory	90	13	28	5		120	10	24	4	
Whooping-cough	1,924	154	155	51	53	2,543	104	426	37	43

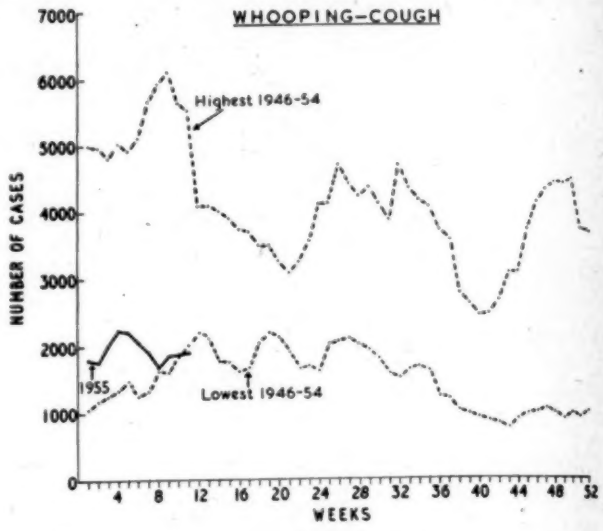
DEATHS in Great Towns	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	1	0		0		1	0		0	
Encephalitis, acute		0	1		0		0	0		0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	3	0	2	0	1	15	0	1	2	2
Influenza	82	10	4	2	15	25	2	3	0	0
Measles		2	1	0	0		0	0	0	0
Meningococcal infection		1	1				0	2		
Pneumonia	458	78	42	24	18	311	40	32	14	7
Poliomyelitis, acute	0	1			0	3	0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	92	15	15	0	9	111	18	17	3	5
Non-respiratory		2	1	0	0			1	1	2
Whooping-cough	2	0	0	0	0	1	0	1	0	0
Deaths 0–1 year	240	30	42	6	14	241	24	39	10	18
Deaths (excluding stillbirths)	7,525	1122	717	156	277	5,943	771	664	149	158
LIVE BIRTHS	8,167	1234	928	215	258	7,953	1180	1059	245	362
STILLBIRTHS	197	18	27			201	15	29		

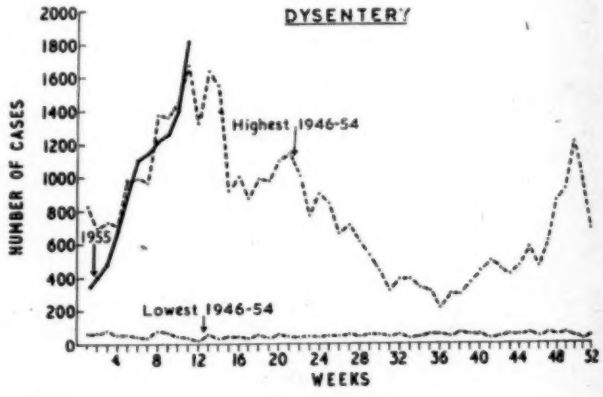
* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

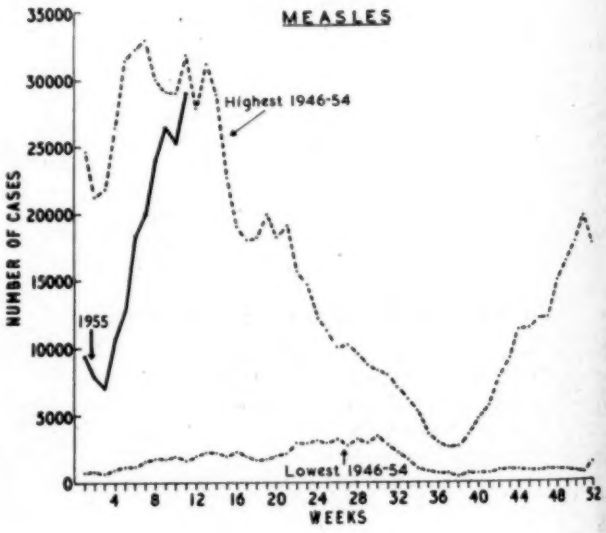
Vital Statistics

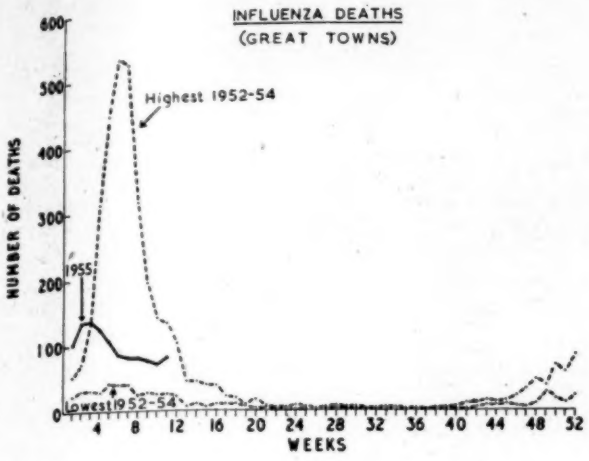
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the nine years 1946–54 (influenza, 1952–4) are shown thus ------, the figures for 1955 thus ————. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

Infectious diseases were more prevalent in England and Wales during the week ending March 19, and the rises in the number of notifications included 3,697 for measles, from 25,321 to 29,018, 409 for dysentery, from 1,407 to 1,816, 59 for scarlet fever, from 780 to 839, and 43 for whooping-cough, from 1,881 to 1,924.

The largest rises in the incidence of measles were 1,059 in London, from 2,626 to 3,685, 365 in Yorkshire West Riding, from 3,737 to 4,102, 364 in Middlesex, from 1,047 to 1,411, 313 in Surrey, from 986 to 1,299, 263 in Northumberland, from 709 to 972, 250 in Warwickshire, from 2,120 to 2,370, 218 in Kent, from 988 to 1,206, 180 in Essex, from 1,905 to 2,085, 178 in Durham, from 808 to 986, 176 in Glamorganshire, from 167 to 343, 174 in Derbyshire, from 879 to 1,053, 146 in Southampton County, from 156 to 302, 141 in Lancashire, from 2,123 to 2,264, and 105 in Staffordshire, from 878 to 983, and the only large fall was 100 in Lincolnshire, from 477 to 377. The only variation of any size in the trends of scarlet fever was a rise of 47 in Yorkshire West Riding, from 57 to 104. The largest fluctuation in the returns of whooping-cough was a decrease of 30 in Cheshire, from 62 to 32. 10 cases of diphtheria were notified, being 1 more than in the preceding week. Areas with multiple cases of diphtheria were Plymouth C.B. 3, Liverpool C.B. 2, Birmingham C.B. 2.

13 cases of acute poliomyelitis were notified, and these were 1 more for both paralytic and non-paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding 5 (Batley M.B. 2), Warwickshire 2 (Birmingham C.B. 2), and London 2 (Hackney 2).

For the eleventh consecutive week a rise has been recorded in the incidence of dysentery, and the number of notifications during the week reached a new record level, being 144 above the previous highest level recorded in 1951. The largest centres of infection during the week were Lancashire 700 (Blackpool C.B. 286, Oldham C.B. 86, Blackburn C.B. 69, Manchester C.B. 69, Liverpool C.B. 49, Chadderton U.D. 33, Middleton M.B. 18, Salford C.B. 15, Lytham St. Anne's M.B. 15, Royton U.D. 14, Failsworth U.D. 10), London 195 (Hackney 103, Shoreditch 33, Islington 14, Stepney 11), Durham 156 (Sedgefield R.D. 56, Felling U.D. 23, South Shields C.B. 15, Gateshead C.B. 11), Northumberland 114 (Newcastle-upon-Tyne C.B. 30, Morpeth M.B. 24, Whitley Bay M.B. 23), Yorkshire West Riding 94 (Leeds C.B. 37, Huddersfield C.B. 21, Sheffield C.B. 11), Leicestershire 90 (Leicester C.B. 62, Melton Mowbray U.D. 13), Norfolk 70 (Norwich C.B. 55), Cheshire 52 (Stockport C.B. 33), Northamptonshire 44 (Northampton C.B. 23, Kettering M.B. 14), Lincolnshire 41 (Scunthorpe M.B. 36), Surrey 39 (Farnham U.D. 26), Yorkshire North Riding 30 (Middlesbrough C.B. 24), and Glamorganshire 25 (Swansea C.B. 12).

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in February was 119, compared with 108 (revised figure) in the previous month and 114 in February, 1954.

The numbers of cases of industrial diseases in the United Kingdom reported during February, 1955, were as follows : lead-poisoning 6, compressed air illness 3, epitheliomatous ulceration 18, chrome ulceration 27 ; total 54. There were no deaths.—*Ministry of Labour Gazette*, March, 1955.

Medical News

Wellcome and Carlsberg Foundations.—At the Apothecaries Hall on April 4 the Wellcome Trustees and directors of the Wellcome Foundation, Ltd., entertained at dinner the members of the Carlsberg Foundation and the management of the Carlsberg Breweries of Copenhagen. Sir HENRY DALE, O.M., F.R.S., chairman of the Wellcome Trustees, presided, in the presence of a distinguished company of guests. The link between the two Foundations is that for all practical purposes their constitution and aims are identical. Both were created with the object of using for philanthropic purposes the whole of the profits of a continuing industrial concern. The Carlsberg Foundation is the senior and came into being in the 1880's following the founding of the Carlsberg Breweries by the late J. C. Jacobsen and their extension by his son. They left the ownership of their breweries to an independent foundation consisting of five eminent Danish citizens appointed by the Royal Danish Academy of Arts and Sciences, whose responsibility it is to apply the profits from the breweries to scientific research and the promotion of the arts, for the benefit of the Danish nation.

Scottish Orthopaedic Council.—On March 21 the Scottish Orthopaedic Council agreed to dissolve. In a statement after the meeting it was pointed out that orthopaedic services were now firmly established in all five regions of Scotland, and therefore the work for which the council was formed has been accomplished. Since its inception in 1942 the council, as the channel through which grants from the Lord Nuffield Fund for Cripples were distributed in Scotland, has disbursed over £24,000 to assist with orthopaedic clinics, educational establishments for crippled children, and other aids for cripples in Scotland. In addition the Nuffield Trustees have made grants amounting to £26,500 for hospital developments at Philipshill, Busby, and Princess Margaret Rose Hospital in Edinburgh. A balance of £17,000, earmarked for orthopaedic developments in Scotland, is to be used for the construction of occupational therapy and workshop departments at the proposed spinal injuries unit at Edenhall, Musselburgh, and to extend the residential training establishment for severely handicapped girls at Anton House, Broughty Ferry.

Kirk Duncanson Fellowship.—The council of the Royal College of Physicians of Edinburgh invites applications for a Kirk Duncanson Research Fellowship of the value of £600 for two years from October 1, 1955. Applicants should submit details of their proposed research and the place where it will be done to the Secretary of the Royal College of Physicians of Edinburgh, 9, Queen Street, Edinburgh 2, before May 7.

Royal Flying Doctor Service.—The QUEEN has honoured Australia's Flying Doctor Service by granting permission for it to be known in future as the "Royal Flying Doctor Service of Australia." An account of the service, given by

Dr. ALLAN VICKERS, the service's senior medical officer, was printed in the *Journal* last year (June 19, p. 1436).

Instruments for Users of Radio-isotopes.—The Scientific Instrument Manufacturers' Association of Great Britain has published a catalogue to help the user of radioactive isotopes in selecting electronic equipment to suit his special needs. The first copy of the catalogue, which is called "Radio Isotope Instrumentation and Accessories," was presented to Sir JOHN COCKCROFT, F.R.S., at a ceremony in London on March 30. Details are given in the catalogue about apparatus for radioactive assay and radiation monitoring and other equipment such as isotope containers and isotope-handling apparatus. Last year, according to figures supplied by the Atomic Energy Research Establishment at Harwell, there were 9,692 orders for radio-isotopes for use in Britain, of which over half came from hospitals, while 6,694 orders were received from abroad. The comparable figures for 1948 were 1,379 and 35. The catalogue may be obtained from the Scientific Instrument Manufacturers' Association, 20, Queen Anne Street, London, W.1.

COMING EVENTS

Westhill Hospital, Dartford.—Postgraduate course for general practitioners, every Thursday afternoon at 2.30 p.m. from April 14 to June 23. Inquiries to Dr. J. C. HOGARTH, Westhill Hospital, Dartford.

Wessex Rahere Club.—Spring dinner on April 30 at the Royal Clarence Hotel, Exeter. Details from Mr. A. DAUNT BATEMAN, 11, The Circus, Bath.

Christian Medical Fellowship.—Two house-parties have been arranged: May 6–9, at the Belsfield Hotel, Bowness, Windermere; and May 20–23 at Linden Hall Hydro, Bournemouth. Details from the Secretary of the Fellowship, 39, Bedford Square, London, W.C.1.

NEW ISSUES

British Journal of Ophthalmology.—The new issue (Vol. 39, No. 4) is now available. The contents include:

SOME OBSERVATIONS ON THE WATER-DRINKING TEST IN GLAUCOMATOUS AND NON-GLAUCOMATOUS SUBJECTS. D. Campbell.
INFLUENCE OF LOCAL ASCORBIC ACID CONCENTRATION ON COLLAGENOUS TISSUE HEALING IN THE CORNEA. T. A. S. Boyd.
THE PRESSURE IN THE CANAL OF SCHLEMM. E. S. Perkins.
VASCULAR SUPPLY OF THE OPTIC PATHWAY. II. FURTHER STUDIES BY MICROARTERIOGRAPHY OF THE OPTIC NERVE. J. François, A. Neetens, and J. M. Collette.
OPHTHALMOLOGICAL COMPLICATIONS OF MULTIPLE MYELOMATOSIS. E. Clarke.
CLINICAL REPORT ON THE RESULTS OF FIFTY CASES OF ROUTINE DACRYOCYSTORHINOSTOMY. G. J. Romanes.
MULTIPLE ISLANDS OF RETINOBLASTOMA. A STUDY OF THEIR INCIDENCE RATE AND THE TIME SPAN OF THEIR APPEARANCE. H. B. Stallard.
CORNEAL INFECTIONS AFTER CORTISONE THERAPY. Y. Mitsui and J. Hanabusa.
OCULAR MANIFESTATIONS IN A CASE OF HAEMORRHAGE INTO THE FOURTH VENTRICLE. M. Sengupta.

Issued monthly; annual subscription £4 4s.; single copy 8s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Tuesday, April 12

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Sir Clement Price Thomas: Resection for Pulmonary Tuberculosis; 6.30 p.m., Professor F. A. R. Stammers: Complications of Gastrectomy.

Wednesday, April 13

HARVEIAN SOCIETY OF LONDON.—8.15 p.m., Sir Adolphe Abrahams, Sir Arthur Porritt, and Dr. Roger Bannister: Medical Aspects of Athletics.
●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Sir Russell Brock: Some Aspects of the Surgical Treatment of Mitral Stenosis; 6.30 p.m., Professor A. M. Boyd: Management of Phlebitis and its Complications.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. A. I. G. McLaughlin: Incidence and Prevention of Dust Diseases in British Industry (illustrated).

Thursday, April 14

BASINGSTOKE PLASTIC CENTRE MEDICAL SOCIETY.—At Rooksdown House (Park Prewett Hospital), Basingstoke, Hants, 7.30 p.m., Professor R. H. S. Thompson: Skin Enzyme Problems in Burns; Dr. W. J. H. Butterfield: Abnormal Carbohydrate Metabolism in Burns; Dr. P. A. Gorer: Serology of Tissue Transfer; Mr. Douglas M. Jackson: Early Primary Surgery with the Use of Homografts; Dr. J. P. Bull: Early Electrolyte and Fluid Balances.
FACULTY OF HOMOEOPATHY.—At Royal London Homoeopathic Hospital, 5 p.m., Dr. H. Fergie Woods: Sciatica; Dr. N. J. Pratt: Analysis of 100 Consecutive Homoeopathic Prescriptions.
INSTITUTE OF PSYCHIATRY.—5.30 p.m., inaugural lecture by Professor H. McIlwain: Maudsley, Mott and Mann on the Chemical Physiology and Pathology of the Mind.
●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. Norman Capener: Hip Joint—Surgical Approaches and Procedures; 6.30 p.m., Mr. V. H. Riddell: Toxic Goitre.

Friday, April 15

BIOCHEMICAL SOCIETY.—At Department of Biochemistry, The University, Liverpool, 11 a.m. (Saturday, April 16, 11.15 a.m.), joint meeting with Association of Clinical Biochemists.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—3.30 p.m., clinical meeting for general practitioners. Mr. W. S. McKenzie: Surgical Treatment of Deafness.
●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Professor Lambert Rogers: Carotid Aneurysms; 6.30 p.m., Mr. J. N. Barron: Skin Grafting for the General Surgeon.

Saturday, April 16

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—10.30 a.m., symposium: Tuberculosis and Other Diseases of the Chest.

APPOINTMENTS

DAVIDSON-LAMB, WILLIAM, *M.C.*, M.B., Ch.B., D.P.H., Deputy County Medical Officer of Health and Deputy Principal School Medical Officer, Gloucestershire County Council.

DEWAR, JOHN, M.B., Ch.B., D.P.H., County Medical Officer of Health, Joint County Council of Moray and Nairn.

GIBSON, JANE ISABELLA, M.B., Ch.B., Consultant Pathologist, Birkenhead and North Wirral Hospital Group (Liverpool Regional Hospital Board).

IRWIN, DAVID, M.B., Ch.B., D.P.M., Deputy Medical Superintendent, St. George's Hospital, Morpeth, Northumberland.

MASON, RICHARD MICHAEL, D.M., M.R.C.P., Consultant Physician to Department of Physical Medicine, The London Hospital, Whitechapel, E.

RAINSFORD, C. R. C., M.D., D.P.H., D.T.M., Medical Officer of Health, Braintree and Bocking and Witham Urban District Councils, and the Braintree and Dunmow Rural District Councils, and Assistant County Medical Officer, Essex.

REID, EDWARD NEIL, M.B., Ch.B., D.P.H., Medical Officer of Health, Kilsyth, Stirlingshire.

RIBCHESTER, MARIE-JOYCE, L.R.C.P.&S.Ed., Assistant Medical Officer of Health (Midwifery and Child Welfare), Blackpool.

RICHARDS, NORMAN A., M.D., M.R.C.O.G., Part-time Consultant Obstetrician and Gynaecologist to the Stafford Group of Hospitals.

SHEMILT, PHILIP, M.B., F.R.C.S., Surgical Consultant, The Military Hospital, Tidworth.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—Joan M. Waterfall, M.B., Ch.B., D.A., Primary F.F.A. R.C.S., temporary Senior Anaesthetic Registrar at Frenchay Hospital, Bristol; Mary F. West, M.B., B.S., D.A. (Part I), Anaesthetic Registrar at Southmead Hospital, Bristol; G. F. Jolly, M.B., B.Chir., M.R.C.O.G., D.Obst.R.C.O.G., Registrar in Obstetrics and Gynaecology at Southmead Hospital, Bristol; Angela D. Fuller, M.B., B.Chir., D.C.H., Paediatric Registrar at Southmead Hospital, Bristol; J. S. Knutzen, M.B., Ch.B., Ear, Nose, and Throat Registrar to the Bath Group of Hospitals; M. J. Gallagher, M.B., B.S., F.R.C.S., Orthopaedic Registrar at Princess Elizabeth Orthopaedic Hospital, Exeter; T. L. Schofield, Ch.M., F.R.C.S., Consultant Surgeon to Bath Clinical Area.

UNIVERSITY COLLEGE HOSPITAL OF THE WEST INDIES.—Dinah J. Hony, M.B., B.S., Registrar in Anaesthetics; Ruth Porter, M.B., Ch.B., D.C.H., Medical Registrar.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Hetherington.—On March 25, 1955, to Monica, wife of Dr. A. W. Hetherington, Redcote, Rainham, Essex, a daughter—Jane Mary.

DEATHS

Dunn.—On March 30, 1955, at 62, Cecil Street, Hillhead, Glasgow, James Churchill Dunn, D.S.O., *M.C.*, D.C.M., M.D., D.P.H.

Mann.—On March 29, 1955, at Drummie House, Letham, Angus, David Mann, M.B., F.R.C.S.Ed.

Nicoll.—On March 17, 1955, at Wonersh, Surrey, James Thomson Bell Nicoll, M.B., Ch.B., aged 55.

Pank.—On March 13, 1955, at Market Rasen, Lincs, Harold William Pank, M.R.C.S., L.R.C.P., aged 80.

Petrie.—On March 17, 1955, at Chertsey Hospital, George Ford Petrie, M.D., of Woking, Surrey, late of Elstree, Herts.

Roe.—On March 17, 1955, at 20, Billing Road, Northampton, Robert Bradley Roe, M.R.C.S., L.R.C.P.,

Scott.—On March 22, 1955, at the Hostel of St. Luke, London, Agnes Catherine Scott, C.B.E., M.B., of Cleeves, France Lynch, Stroud, Glos, aged 79.

Sharp.—On March 18, 1955, Alexander Sharp, C.B., C.M.G.T.D., F.R.C.S.Ed., Colonel, A.M.S., retired.

Thomas.—On March 21, 1955, at Addenbrooke's Hospital, Cambridge, John Glyndor Treharne Thomas, *M.C.*, M.R.C.S., L.R.C.P., D.P.M., of 353, Hills Road, Cambridge, aged 62.

Thorp.—On March 16, 1955, at Bafford Cottage, Charlton Kings, Cheltenham, Glos, Henry Thorp, M.Sc., M.B., Ch.B., formerly of Lymm, Cheshire.

Wallis.—On March 16, 1955, William Evershed Wallis, M.B., B.Ch., of Oakhurst, East Grinstead, Sussex, aged 71.

Woodward.—On March 22, 1955, at Coventry, Herbert Croker Sperling Woodward, M.B., B.C., of Kingston Bagpuize, Abingdon, Berks, aged 86.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Wet Clothes

Q.—*What, in healthy people, are the disadvantages of getting wet, and staying in wet clothes? How is the picture modified by atmospheric temperature, relative humidity, amount of clothing, and regular use of soap and hot water in washing? Primitive people, even the malnourished, appear to get wet and stay wet for long periods without discomfort or subsequent ill effect.*

A.—Presumably the questioner is thinking of the old advice: "You must get those wet clothes off before you catch your death of cold." It is doubtful if wearing wet clothes ever gave anyone a cold; but when the outer garments are wet there is evaporation from them and the surface temperature of the outside clothing will fall below that of the surrounding air, possibly to the wet-bulb temperature. The temperature gradient from the skin to the outer surface of the clothing is therefore increased; at the same time the replacement of the insulating air between the fibres of the cloth by non-insulating water will decrease the thermal insulation of the clothing. These two factors together cause a man in wet clothing to lose heat more rapidly to the environment than a man in dry clothes. Skin temperature and later even body temperature may fall. It has been said that when the body temperature does fall there is diminished local resistance to infection, especially in the nasopharyngeal tract (although experimental work has failed to confirm this). To this extent, therefore, wearing wet clothing might contribute to catching a cold, but the cold infection has got to be there to be caught.

Atmospheric temperature and humidity have an effect inasmuch as these two factors govern the wet-bulb temperature. For physical reasons the surface temperature of the wet clothing can never fall below the wet-bulb temperature, and the higher the humidity the nearer does the wet-bulb temperature approach the atmospheric dry-bulb temperature. At high humidities therefore the skin surface gradient is less affected than at low humidities.

The more clothing worn, within limits, the warmer the skin, so long as the clothing is dry. If this clothing suddenly becomes soaked and so loses all its insulation the thermal gradient from the skin to the surface of the clothes will be very steep and heat loss will be rapid. When very little clothing is worn the skin temperature may be almost the same in the clothed as in the unclothed areas, and wetting the clothing will then make very little difference.

The regular use of soap and water, according to O'Brien,[1] predisposes to prickly heat and allied skin conditions, as it removes the natural fats of the skin. As prickly heat and intertrigo are more likely to develop in damp areas of skin, it is possible a well-washed individual might suffer more in this respect if he had to live in wet clothes than one of the "great unwashed." The questioner may also be thinking of the value of grease as thermal insulation. It has been found experimentally, however, that in immersion experiments the minimum thickness of grease on the skin which will have any effect on the rate of cooling is 1.8 mm. This represents 2.7 litres of grease for an average-sized man—and a mighty long time between baths.

I doubt if primitive men are any better able to withstand the purely physical effect of wearing wet clothes than are others; but they may be better prepared to put up with the discomfort, as they may have no alternative. On the other hand, a primitive man may be wearing fewer clothes, with the advantage already noted, or he may even take all his clothes off. Once clothes are wet right through their insulation value is almost nil, and a naked man is actually better off, as the area from which evaporation can take place may be 25% less. The really important thing here is knowing what to do when one's clothes do get wet. The old Scots shepherds were said to turn their plaids wet side in when the rain stopped; in this way they stopped excessive evaporation and consequent cooling. Changing wet socks for dry socks, even though the boots are still wet, restores the insulating power of the sock and is also a great comfort; it is both physically and physiologically justified.

REFERENCE

[1] *Brit. J. Derm.*, 1947, **59**, 125.

Ringworm

Q.—*In treating a case of ringworm affecting the groins, axillae, and toes, should the fungicide be applied widely to all areas showing scaling (such as between the toes) irrespective of whether inflammation is present or not? What disinfection of clothes and bedding is advised? How should the bathroom floor (made of wood) be disinfected?*

A.—Fungicide should be applied to all areas where there is scaling.

Bed linen is disinfected by the usual process of washing, and most types of underclothing can be boiled. The feet of socks or stockings are probably best sterilized by soaking in lysol or some similar disinfectant before they are washed.

For the disinfection of a wooden floor, scrubbing with soap and water would probably be efficient.

Dangers of Adrenaline During Prostatectomy

Q.—*What is the risk of injecting adrenaline into the prostatic bed prior to performing a prostatectomy? Would you consider 1.5 ml. adrenaline (1 in 1,000) diluted with 40 ml. of saline to be a small, medium, or a large dose? General anaesthesia is used, but trichlorethylene, cyclopropane, and chloroform are avoided.*

A.—There is some risk that in injecting adrenaline solution into the prostatic bed some or all of it might get into the circulation. If this did happen 1.5 ml. of adrenaline would be a large dose for anybody. Little is gained by making the dilution of adrenaline intended for vasoconstriction much stronger than 1 in 100,000. If the whole 40 ml. of solution is to be injected, the required dilution is obtained by mixing 0.5 ml. of adrenaline in 50 ml. saline. Few genito-urinary surgeons require this volume for the purpose described. Usually a few ml. only of the solution is injected into two or three points in the prostatic capsule. In these circumstances the stronger solution mentioned in the question may be used, since the dose of adrenaline would then be kept to about 0.5 ml., a reasonably safe dose.

The risk of sudden death due to adrenaline is present with any form of anaesthetic; it is probably increased in the case of the three anaesthetic agents mentioned in the question.

Hitch-hiking to Australia

Q.—*Two patients of mine are shortly hitch-hiking to Australia via Yugoslavia, Greece, Turkey, Syria, Iraq, India, Pakistan, Singapore, Burma, and Indonesia. Can you please tell me what inoculations and vaccinations they should have before starting on this journey? Can you also tell me what antimalarial drug is advised, in what doses, and during what part of the journey should this be taken? Are any other health precautions advised?*

A.—Travellers are required by international law to be vaccinated against smallpox, and must be in possession of a valid international certificate of vaccination. As these particular travellers are going through India and Pakistan they

should also be vaccinated against cholera; this, too, is legally required as a condition of entry into these countries. Although vaccination against the enteric group of fevers is not required by law, it is advisable to have this done. There is no special order in which the above vaccinations should be carried out. Vaccination against yellow fever is legally required of those travelling to tropical Africa or America, and it is recommended that this be done at least four days before smallpox vaccination if this is also required.

The most effective antimalarial prophylactics are proguanil in doses of 100 mg. daily and chloroquine in doses of 300 mg. (base) weekly. It would be advisable to start taking the prophylactic on reaching the Mediterranean littoral and to continue thereafter throughout the journey and for three weeks after entering the non-malarial region at the end of the journey.

Among other health precautions the most important is the use of safe water supplies, and if safety cannot be guaranteed water should be boiled. Salads and other uncooked foods should be avoided. A valuable book, designed for the lay reader and dealing with general health problems in the Tropics, is *Health and Disease in the Tropics*, by Charles Wilcocks, published by Oxford University Press, price 15s. The Ross Institute, c/o London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1, also issue a pamphlet entitled "Notes on the Preservation of Personal Health in Warm Climates."

Constant Sexual Urge in an Old Man

Q.—*I have a patient in his late eighties with a moderately enlarged prostate who is tormented with an almost constant sexual urge. He is impotent. Frequency of micturition is the only other symptom. Would oestrogen therapy help?*

A.—Although it is possible that stilboestrol in a dose of 5 mg. daily might diminish the sexual urge, it is unlikely to do so if erections do not occur. Probably the best treatment would be prostatectomy if the other symptoms justify it.

Hairy Tongue

Q.—*During the last six months in this practice I have seen an increasing number of hairy tongues, with and without glossitis. Some have been present for only a few days or months, others for years or even for life. (a) Are several clinical types of hairy tongues recognized? (b) What is their cause? (c) Has there been a recent increase in the incidence of the condition?*

A.—There are probably at least four types of black hairy tongues with differing aetiologies: (1) congenital and familial, when the condition is present from birth and is sometimes known as ichthyosis of the tongue; (2) parasitic, when it is due to various micro-organisms (yeasts, particularly *Candida albicans*, actinomycetes, and microbacilli); (3) the result of chemical irritants, such as toothpaste, mouthwashes, and disinfectants; (4) following the local or systemic use of antibiotics, particularly chlortetracycline ("aureomycin").

It is difficult to say whether there has been an increase in the incidence of the condition in recent years, because we see only a small proportion of those afflicted with this benign malady. The literature and personal experience suggest that there has been an increase in the incidence of hairy tongue, and that antibiotics, particularly those of the tetracycline group, are responsible for this increase, as many patients develop the condition towards the end of, or shortly after, a course of one of these drugs.

Lozenges containing antibiotics are more likely to produce black tongues, and they have also followed the use of an ointment containing chlortetracycline on the lips.

A number of cases arise spontaneously, and recently studies of the tongue with Wood's light have shown that the flora of the dorsum of the tongue may change very rapidly in the apparently normal, healthy mouth, so that it is not surprising that occasionally a brown tongue follows this spontaneous change in the flora. With increasing use of mouthwashes, antibiotic drugs, toothpastes containing various chemicals, and the like, it is probable that the condition will be more frequently met with in the future.

Cigarette Stains on the Fingers

Q.—*How can one take off nicotine stains from hands and mouth of heavy cigarette-smokers, without irritation to the skin? Attempts with hydrogen peroxide, up to 20%, and 10% sodium hypochlorite solution have been only partially successful.*

A.—It is presumed that these stains are caused not only by nicotine but by tar as well, though I have no precise information on this point. The stains can be removed comparatively easily with pumice stone, and it is probably better to do this periodically than to make frequent applications of strong chemicals to the skin. However, the use of a cigarette holder will prevent most of this staining.

NOTES AND COMMENTS

Thiourea.—Dr. J. H. PETERS (Atlanta, U.S.A.) writes: In answering a question regarding thiourea ("Any Questions?" November 13, 1954, p. 1179), it is stated that the compound had been administered in 1–2 g. daily doses and was abandoned in favour of "more active . . . compounds" and because it was unpleasant to take and imparted an odour to the breath. Actually, thiourea has been used successfully for therapy of hyperthyroidism, administered in quite low (70–280 mg. per day) doses, displays relatively little toxicity, and is pleasant to take.[1 2 3 4] The authors of these investigations reported halitosis only when the drug was given intravenously. Actually the early abandonment of thiourea in favour of other goitrogens was due to a combination of factors. One was that early investigators did set dosages too high and experienced the difficulties mentioned in your answer. In the meantime, the introduction of propylthiouracil, and later of aminothiazole, proved to be so successful that thiourea, which may actually be less toxic than either, has been ignored. I pass this information to you lest readers might consider using the compound in excessive doses in cases not tolerating other goitrogens.

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1 Darrowski, T. S., Man, E. B., and Winkler, A. W., *Amer. J. med. Sci.*, 1945, **210**, 777.
2 —— —— —— *J. clin. Invest.*, 1946, **25**, 597.
3 —— —— —— ibid., 1947, **26**, 446.
4 —— —— Elkington, J. R., Peters, J. P., and Winkler, A. W., *Amer. J. med. Sci.*, 1947, **215**, 123.

OUR EXPERT writes: This additional information on the administration of thiourea to man should help to allay any remaining fears about the possible harmful effects of traces of thiourea present in oranges.

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